

Caution and clarity required in the use of chloroquine for COVID-19

As the coronavirus disease 2019 (COVID-19) outbreak continues to spread rapidly, efforts are ongoing in China and around the world to develop effective treatments. Among the drugs being tested for COVID-19 in China is chloroquine, which was reported on Feb 4, 2020, to inhibit severe acute respiratory syndrome coronavirus 2 in vitro. The drug was rapidly pushed to clinical testing as an experimental treatment in China; on Feb 15, 2020, it was included in the sixth version of the COVID-19 treatment guidelines by the National Health Commission of the People's Republic of China. This guideline established the use of chloroquine nationwide for patients with COVID-19, at a recommended adult dose of 500 mg twice per day for no more than 10 days.¹

The lethal dose of chloroquine in adults is about 5 g.² In the human body, chloroquine has a large volume of distribution with an elimination half-life of 20–60 days and a tendency to accumulate in metabolically active tissues at higher levels compared with the plasma concentration.^{3,4} In view of these properties, the recommended dose of 500 mg twice per day can quickly approach danger thresholds with sustained use. At the maximum course of 10 days, this regimen is substantially more aggressive than recommended regimens for the use of chloroquine as an antimalarial. The effects of chloroquine poisoning are well documented and include retinopathy and immunosuppression, with contraindications in several conditions including pregnancy.³ On Feb 26, 2020, the treatment guidelines were revised, shortening the maximum course to 7 days while recommending a lower dose for patients weighing less than 50 kg and highlighting contraindications

including pregnancy.⁵ It is encouraging that an appropriate adjustment with improved consideration for the toxicological properties of the drug was made so quickly given the urgency of the situation. However, we advise continued caution in bringing new treatments to clinical use in such a rapid manner. Recommended doses should be established with close reference to pharmacological profiles and side-effects must be closely monitored. The less toxic hydroxychloroquine should also be considered as an alternative. Finally, the potential toxicities of experimental treatments should be meticulously reported in peer-reviewed publications to avoid potentially misleading accounts and the risk of dangerous self-medication by the public. The rapid identification and development of such novel treatments is encouraging and will be instrumental in the battle against COVID-19, as long as prudence and rigour continue to be practised in both implementation and reporting.

We declare no competing interests.

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