Hydroxychloroquine use during the COVID-19 pandemic 2020

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AUSTRALIA IS EXPERIENCING a pandemic of severe acute respiratory syndrome (SARS) due to the virus SARS-CoV-2, for which there is no vaccine and no proven antiviral treatment. Repurposed hydroxychloroquine has been suggested as treatment, and some practitioners are using it off-label; however, this is not evidence based, and high doses of hydroxychloroquine can be associated with significant side effects.

COVID-19 first emerged in Wuhan, China, in December 2019, probably from zoonotic origin. It spread rapidly and was declared a pandemic by the World Health Organization on 12 March 2020. Disease features are often mild (80%), but up to 5% of cases develop severe disease with respiratory failure or multi-organ dysfunction. As yet, there is no specific antiviral treatment available, and treatment is limited to supportive care, including ventilatory support.

Chloroquine and its less toxic derivative hydroxychloroquine were originally used as anti-malarial agents, but were subsequently repurposed for autoimmune diseases in rheumatology and dermatology. The mechanism of action of anti-malarial agents in autoimmune conditions remains unclear, but it is probably multifactorial and includes immunomodulatory and anti-inflammatory effects on the host.

Off-label use of anti-malarial agents was first suggested as treatment for SARS following the epidemic in 2002–03 in Asia, after hydroxychloroquine-related compounds[1] were shown to have SARS coronavirus antiviral activity in vitro. Recently, chloroquine[2] and hydroxychloroquine[3] have also been found to have antiviral effects on COVID-19 in vitro, including inhibition of viral entry and post-entry stages of infection. The authors proposed treatment with hydroxychloroquine; however, it was not clear whether treatment was recommended as prophylaxis or for established SARS-CoV-2 infection.[3]

There are very limited data from controlled human trials of hydroxychloroquine treatment for SARS-1 or COVID-19. Gautret et al treated 26 patients infected with SARS-CoV-2 with hydroxychloroquine and showed a decreased viral load in nasopharyngeal swabs; however, this study was limited by small patient numbers and a high dropout rate.[4]

Hydroxychloroquine treatment is generally well tolerated, and side effects are usually dose and duration related, but treatment can be complicated by adverse events. Dermatological, gastro-intestinal and neurological side effects are the most common; retinal and cardiac side effects (long QT interval) are less common but carry significant morbidity. With usual dosing (≤5.0 mg/kg), retinopathy occurs in up to 3.5% of individuals taking hydroxychloroquine, rising to 7.5% after 10 years.[5] However, retinopathy has been reported as early as after nine months with higher doses. Most patients with early retinopathy have no symptoms, while a minority experience glare or difficulty reading. Retinopathy symptoms typically develop late, thus the absence of symptoms does not rule out early irreversible toxicity.

At present, there are no studies demonstrating the clinical efficacy of hydroxychloroquine for the prophylaxis or treatment of COVID-19 infection. In the meantime, medical practitioners are urged **not** to prescribe hydroxychloroquine off-label in the current pandemic because of the lack of evidence and the risk of depleting stocks of the medication for other indications. Practitioners are reminded that there is a significant risk of retinal toxicity if patients take this medication in high doses for prolonged periods of time without ophthalmic supervision.

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