Received: 21 April 2020 | Revised: 16 May 2020 | Accepted: 18 May 2020

DOI: 10.1111/apa.15373

ACTA PÆDIATRICA NURTURING THE CHILD WILEY

A DIFFERENT VIEW

Efficacy, safety and cost-effectiveness of hydroxychloroquine in children with COVID-19: A call for evidence

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1 | COVID-19: AN URGENT PROBLEM WITH LIMITED TREATMENT OPTIONS

The novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic poses a serious threat to public health and local economies around the globe. This has created an urgent need to identify effective medications for its prevention and treatment.[1] Among these treatments, the off-label use of hydroxychloroquine (HCQ), a less toxic derivate of chloroquine, has become a common practice among clinicians, including paediatricians, despite lack of evidence of its clinical efficacy for this indication (especially for paediatric patients) at present time.[2]

Hydroxychloroquine is an attractive option as it has been shown to have in vitro antiviral and immunomodulatory activities, there is considerable experience of its use in a range variety of acute and chronic paediatric and adult diseases, and it has relatively low cost and availability.[3] It is also accumulated in the lungs (and other tissues), achieving concentrations 200-700 times higher in the lungs than in plasma, and the expectation is that it would act to inhibit SARS-CoV-2 infection.[4,5] There is preliminary albeit controversial evidence showing that HCQ might shorten the duration of the viral shedding.[6] Although it is generally accepted that children are at less risk of serious illness and aggressive clinical course, younger age may be associated with a longer duration of viral shedding.[7] It is theoretically desirable to target a reduction in the duration of viral shedding, as this could limit the community spread of SARS-CoV-2 and to prevent the transmission of the virus to high-risk adults and healthcare workers.

However, it is not yet clear if the benefits outweigh the risks. The majority of children will have mild symptoms, and widespread use of hydroxychloroquine may confer only minimal benefit. There are concerns with the safety profile of HCQ, and many uncertainties around dosing for this indication, particularly in children.[8] Furthermore, it is important to consider the cost-effectiveness of any intervention used during the COVID-19 pandemic. In low-, middle- and high-income settings, resources such as personal protective equipment (PPE) and intensive care supplies may be in short supply. Informed choices may need to be made in prioritising the most cost-effective interventions, pharmacological or not, at individual and societal level. As the pandemic draws to a close, the societal and economic impact of COVID-19 will have generational effects on child health and well-being. The reversal of this will require a systemic and concerted effort at national and international level.

2 | THERE IS A NEED FOR MORE EVIDENCE IN CHILDREN

To this date, there are over 158 registries on ICTRP COVID-19 database assessing hydroxychloroquine or chloroquine as a treatment or prophylactic intervention in COVID-19 patients and they are planning to enrol over 130.000 participants.[9] Despite this huge number in trials and expected participants, only a few are recruiting children. We would therefore encourage nations where the undertaking of high-quality clinical trials in children during the current SARS-CoV-2 pandemic is possible, to ensure that putative treatments that would be available and affordable in low- to middle-income countries (LMICs), such as hydroxychloroquine, are included wherever possible. This will help ensure that robust evidence about the risks and benefits to children themselves, as well as the population as a whole, are considered and provide worldwide impact. These trials should be reported in a way that enables robust meta-analysis and cost-effectiveness analysis. At a time of great uncertainty, evidence is urgently needed to inform treatment options, and therefore, randomised controlled trials are necessary to clarify further the clinical benefit of HCQ in paediatric patients with SARS-CoV-2 infections. However, it is important to note that despite the fact that reliable and interpretable efficacy and safety data for a certain medication can only be obtained by means of appropriate planned and conducted clinical trials, the decision to conduct such trials should be made only after careful consideration of a reasonable relationship between calculated (acceptable) risks and anticipated benefits, if any.[10]

ACKNOWLEDGEMENTS

This is a summary of independent research carried out at the National Institute for Health Research (NIHR), Alder Hey Clinical Research Facility. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.

CONFLICT OF INTEREST

Nothing to declare.

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How to cite this article: Rodríguez-Martínez CE, Fernandes RM, Hawcutt DB, Sinha IP, Pacheco RL. Efficacy, safety and cost-effectiveness of hydroxychloroquine in children with COVID-19: A call for evidence. *Acta Paediatr*. 2020;109:1711–1712. https://doi.org/10.1111/apa.15373