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Title: ECG evolution after hydroxychloroquine treatment in acute rheumatic fever - data from HYDRxARF

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Background & Aims: An effective immunomodulator to suppress the carditis of acute rheumatic fever (ARF) would reduce the subsequent severity of chronic rheumatic heart disease. Hydroxychloroquine (HCQ), a candidate immunomodulator, in-vitro blocks dysregulated T helper cells in ARF. HYDRxARF is an open-label proof of concept and safety study using HCQ for ARF in Aotearoa, New Zealand. First degree atrio-ventricular block occurs commonly in ARF, and advanced AV block occurs not infrequently. The QTc may also be prolonged but this is almost invariably a benign finding. During the COVID-19 pandemic, the use of high dose HCQ in adults raised concerns of acute myocardial toxicity.

Methods: 22 patients with ARF and carditis were consented to receive oral HCQ at 5-7mg/kg/day for 4-6 weeks We planned inpatient observation > 1 week from enrolment for potential side effects and serial ECGs. HCQ was not commenced or withheld if there was a significant rise in QTc as per the study protocol based on the guidelines of the Mayo clinic for QT prolonging medications. Repeat ECGs were taken at 48 hours, 4-5 days, 7 days and 2-3 weeks, 6 weeks and 6 months. The PR interval, QRS duration and QTc were also calculated serially.

Results: The mean (SD) PR interval for the cohort was 180 (43.9) milliseconds. 12 patients had first degree atrioventricular block by age. There was no further prolongation of the PR interval after HCQ. QTc data: 91% (20/22) commenced HCQ at enrolment with baseline QTc in a 'safe' range. 8 patients had severe carditis, two of whom had prolonged QTc for age and gender and they did not start HCQ for 8 days and 11 days respectively until their QTc evolved into a 'safe' range. One patient had a 37ms rise in QTc between day 5 and day 7 , it fell by 10 ms 3 days later and HCQ was continued. No other patient had recognised prolongation of QTc after commencing HCQ. Serial median and IQR for QTc for cohort data is shown in the graph. No ventricular tachycardia was observed.

Serial QTc data (median and IQR) is presented in the figure below.

Conclusions: In this proof of concept and safey study, HCQ at the standard paediatric dose of 5-7mg/kg did not prolong the QTc in the setting of ARF in this initial cohort. HCQ may need to be initially withheld for some patients with prolonged QTc due to ARF, usually in those with severe carditis, until the QTc evolves into the normal range. No ventricular tachycardia was observed. There was no apparent effect of HCQ on the PR interval.