Response to: ‘Antimalarial use and arrhythmias in COVID-19 and rheumatic patients: a matter of dose and inflammation?’ by Erre et al

We read the comment by Erre et al to our correspondence about hydroxychloroquine (HCQ) use during the COVID-19 pandemic with great interest.1,2 As also highlighted by others, antimalarial use such as HCQ during the COVID-19 pandemic has the potential for cardiotoxicity.1,3 Patients with COVID-19 and those with rheumatic disease represent distinct populations with different dosing strategies. We agree that the potential for cardiotoxicity from antimalarials may also be different related to these issues.

The authors present interesting data on QTc intervals in patients with rheumatoid arthritis (RA) on maintenance HCQ, drawn from an established cohort of patients without known significant underlying cardiovascular disease. While these patients had statistically significant higher QT intervals on HCQ compared with those on other disease-modifying antirheumatic drugs (DMARDs), the mean remained within normal limits so this difference is unlikely to have a large clinical impact. Therefore, it appears that the QTc interval is not pathologically prolonged among patients with RA on maintenance HCQ. While it is possible that HCQ may affect risk for a small proportion of patients with rheumatic diseases, perhaps with borderline or unrecognised QTc prolongation or other cardiac disorders, we find these data reassuring. Despite widespread use in rheumatic diseases, pathological QTc prolongation has not been recognised as a complication of HCQ.

Another group of investigators recently studied pre-QTc and post-QTc interval measurements among hospitalised patients with COVID-19 who received at least 1 day of HCQ, with or without azithromycin.3 Their patients studied had a similar mean age to those reported by Erre et al (60 years), though 10% had coronary artery disease. Of the 37 who received HCQ monotherapy, 19% developed prolonged QTc of 500 ms or more. Of the 53 who received HCQ with concomitant azithromycin, incidence of prolonged QTc was 21%. Compared with baseline values, those receiving HCQ alone had a mean QTc increase of 5.5 ms, while those who received combination HCQ and azithromycin had a mean QTc increase of 23 ms. Among all 90 patients, 28% had elevated troponin levels consistent with acute cardiac injury. Therefore, patients infected with COVID-19 may be particularly susceptible to QTc prolongation with HCQ use related to several factors such as higher dose of HCQ, high levels of systemic inflammation, ongoing cardiac injury and concomitant use of other QTc prolonging medications such as azithromycin. A recent observational study among hospitalised patients with COVID-19 associated combined HCQ and azithromycin use with increased risk of cardiac arrest compared with use of neither drug, also highlighting this concerning possible cardiotoxicity of HCQ among that patient population.4

While we caution against strong inference, these data justify continued investigation regarding the cardiotoxicity of antimalarials specifically in COVID-19. We agree with the authors that reports of potential cardiotoxicity of HCQ in COVID-19 should not be extrapolated to patients with rheumatic disease where its safety is well established.

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