

Hydroxychloroquine-associated QT interval prolongation

Treatment with hydroxychloroquine in patients with coronavirus disease 2019 (COVID-19) is associated with a risk of rate-corrected QT (QTc) interval prolongation, which is greater with concomitant azithromycin treatment, according to findings of a US study published in *JAMA Cardiology*.¹

This study investigated the risk of QT interval prolongation in patients with COVID-19 who were treated with hydroxychloroquine alone (n=37) or hydroxychloroquine plus azithromycin (53) between March and April 2020 in a tertiary centre in Boston, Massachusetts. The most frequent comorbidities were hypertension (53%) and diabetes mellitus (29%).

Patients treated with hydroxychloroquine alone had a higher median QTc interval at baseline than those treated with hydroxychloroquine plus azithromycin (455 vs 442 msec; $p < 0.001$). However, the change in QTc interval was greater in patients who received the drug combination than in those who received hydroxychloroquine alone (median 23 vs 5.5 msec; $p = 0.03$).

QTc interval prolongation was ≥ 500 msec in 19% of patients who received hydroxychloroquine alone versus 21% of patients who received concomitant azithromycin, and the QTc interval increased by ≥ 60 msec in 3% versus 13%. The risk of QTc interval prolongation was higher in patients receiving loop diuretics (adjusted odds ratio [aOR] 3.38; 95% CI 1.03, 11.08) and those with QTc interval ≥ 450 msec (aOR 7.11; 95% CI 1.75, 28.87).

Hydroxychloroquine was discontinued in nine patients due to intractable nausea or hypoglycaemia, and in one patient because of torsades de pointes during treatment with hydroxychloroquine plus azithromycin.

"Clinicians should carefully weigh risks and benefits if considering hydroxychloroquine and azithromycin, with close monitoring of QTc and concomitant medication usage," said the authors.

The use of hydroxychloroquine with or without azithromycin increases the QTc interval in the majority of patients with COVID-19 who are in an intensive care unit (ICU), according to findings of a French study published in a research letter in *JAMA Cardiology*.²

Forty patients with COVID-19 who were admitted to an ICU in Lyons, France, received hydroxychloroquine alone (55%) or with azithromycin (45%); 50% of patients also received other drugs with a known or possible risk of QTc interval prolongation.

Treatment with hydroxychloroquine with or without azithromycin increased the QTc interval in 93% of patients. Overall, QTc interval was prolonged in 36% of patients: the QTc interval increased by ≥ 60 msec in ten patients and QTc interval prolongation was ≥ 500 msec in seven patients. The incidence of QTc interval prolongation ≥ 500 msec was greater in patients who received hydroxychloroquine plus azithromycin than in those who received hydroxychloroquine alone (33% vs 5%; $p = 0.03$).

"The finding that QTc intervals increased in more than 90% of patients raises concerns about the widespread use of hydroxychloroquine, with or without azithromycin, to treat COVID-19 in settings where patients cannot be adequately monitored," commented the investigators.

"These reports . . . provide concordant insights regarding the potential for QT prolongation with this treatment in patients hospitalized with COVID-19," said Dr Robert Bonow, Editor of *JAMA Cardiology*, and colleagues in an accompanying editorial published in *JAMA Cardiology*.³ The data "underscore the potential risk associated with widespread use of hydroxychloroquine and the combination of hydroxychloroquine and azithromycin in ambulatory patients with known or suspected COVID-19," they said.

1. Mercurio NJ, et al. Risk of QT Interval Prolongation Associated With Use of Hydroxychloroquine With or Without Concomitant Azithromycin Among Hospitalized Patients Testing Positive for Coronavirus Disease 2019 (COVID-19). *JAMA Cardiology* : 1 May 2020. Available from: URL: <http://dx.doi.org/10.1001/jamacardio.2020.1834>.

2. Bessiere F, et al. Assessment of QT Intervals in a Case Series of Patients With Coronavirus Disease 2019 (COVID-19) Infection Treated With Hydroxychloroquine Alone or in Combination With Azithromycin in an Intensive Care Unit. *JAMA Cardiology* : 1 May 2020. Available from: URL: <http://dx.doi.org/10.1001/jamacardio.2020.1787>.

3. Bonow RO, et al. Hydroxychloroquine, Coronavirus Disease 2019, and QT Prolongation. *JAMA Cardiology* : 1 May 2020. Available from: URL: <http://dx.doi.org/10.1001/jamacardio.2020.1782>.