Smartphone electrocardiogram for QT interval monitoring in Coronavirus Disease 2019 (COVID-19) patients treated with Hydroxychloroquine

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ABSTRACT

Introduction: The global pandemic of Corona Virus Disease 2019 (COVID-19) has led to the re-purposing of medications, such as hydroxychloroquine and lopinavir-ritonavir in the treatment of the earlier phase of COVID-19 before the recognized benefit of steroids and antiviral. We aim to explore the corrected QT (QTc) interval and 'torsadogenic' potential of hydroxychloroquine and lopinavir-ritonavir utilising a combination of smartphone electrocardiogram and 12-lead electrocardiogram monitoring.

Materials and Methods: Between 16-April-2020 to 30-April-2020, patients with suspected or confirmed for COVID-19 indicated for in-patient treatment with hydroxychloroquine with or without lopinavir-ritonavir to the Sarawak General Hospital were monitored with KardiaMobile smartphone electrocardiogram (AliveCor®, Mountain View, CA) or standard 12-lead electrocardiogram. The baseline and serial QTc intervals were monitored till the last dose of medications or until the normalization of the QTc interval.

Results: Thirty patients were treated with hydroxychloroquine, and 20 (66.7%) patients received a combination of hydroxychloroquine and lopinavir-ritonavir therapy. The maximum QTc interval was significantly prolonged compared to baseline (434.6±28.2msec vs. 458.6±47.1msec, p=0.001). The maximum QTc interval (456.1±45.7msec vs. 464.6±45.2msec, p=0.635) and the delta QTc (32.6±38.5msec vs. 26.3±35.8msec, p=0.658) were not significantly different between patients on hydroxychloroquine or a combination of hydroxychloroquine and lopinavir-ritonavir. Five (16.7%) patients had QTc of 500msec or more. Four (13.3%) patients required discontinuation of hydroxychloroquine and 3 (10.0%) patients required discontinuation of lopinavir-ritonavir due to QTc prolongation. However, no torsade de pointes was observed.

Conclusions: QTc monitoring using smartphone electrocardiogram was feasible in COVID-19 patients treated with hydroxychloroquine with or without lopinavir-ritonavir. The usage of hydroxychloroquine and lopinavir-ritonavir resulted in QTc prolongation, but no torsade de pointes or arrhythmogenic death was observed.

KEYWORDS:
Coronavirus disease 2019, hydroxychloroquine, lopinavir-ritonavir, long QT, torsade de pointes, smartphone electrocardiogram

INTRODUCTION

The global pandemic of coronavirus disease 2019 (COVID-19) has led to the "off label" re-purposing of medications, such as chloroquine, hydroxychloroquine, azithromycin, and lopinavir-ritonavir for COVID-19.[1,2] The latest National Institute of Health (NIH) guidelines had recommended against the use of the abovementioned medications following studies that showed equivocal or non-beneficial results. However, they were commonly used during the initial phase of the outbreak.[3] These medications are potentially associated with drug-induced torsade de pointes (DI-TdP) and sudden cardiac death through prolongation of QT interval which necessitates close electrocardiography monitoring.[4]

The mechanism of QT prolongation is due to the inhibition of human-Ether-a-go-go Related Gene (hERG), which is a subunit of the I_{Kr} channel, or aggravating the late sodium channel (I_{NA-L}) during the early depolarisation phase, leading to prolong QT interval. Risk factors contributing to the increased risk of DI-Tdp have been validated by Tisdal et al.[5] Study on QT interval prolongation associated with the use of hydroxychloroquine with or without azithromycin has been reported by Mercuro and co-workers[6] and Bessière and co-workers.[7] However, the QT-prolonging potential of hydroxychloroquine and lopinavir-ritonavir in COVID-19 patients, whether as a single agent or in combination, has never been described before.

The SARS-CoV-2 virus has a high risk of transmission via respiratory secretions and to a lesser extent, contact. There had been reports of healthcare personal being infected with the virus in the line of service.[8] Thus, there was major concern regarding the safety and exposure of healthcare personal conducting regular 12-lead electrocardiogram monitoring for QT interval during the widespread use of QT-prolonging medications. KardiaMobile smartphone electrocardiogram (AliveCor®, Mountain View, CA) was suggested as an alternative to a 12-lead electrocardiogram in monitoring the QT intervals.[4] Although it seems to be a feasible recommendation, the utility of this method has never been

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