Brian maurer young investigator award finalists 2020

1 COVID-19 AND QTc: IS HYDROXYCHLOROQUINE WORTH THE RISK? A REVIEW OF QT PROLONGATION IN HOSPITALISED COVID-19 PATIENTS TREATED WITH HYDROXYCHLOROQUINE AND AZITHROMYCIN

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Background Hydroxychloroquine (HC) and Azithromycin (AZ) is a novel treatment regimen in the management of Coronavirus disease 2019 (COVID-19). Both HC and AZ are associated with QT prolongation, which can precede malignant arrhythmias such as torsade de pointes (TdP) and ventricular fibrillation. Limited literature exists to establish the incidence of QT prolongation, with morbidity and mortality. This study was performed to assess the incidence of QT prolongation secondary to HC and AZ, and how it related to morbidity and mortality.

Methods A retrospective chart review was performed of COVID-19 patients treated with HC, with or without concomitant AZ, in our hospital in March and April 2020. Their baseline demographic characteristics and co-morbidities were recorded. The baseline corrected QT interval (QTc) and change in QTc was calculated using Bazett’s formula on both electrocardiograms (ECGs) and inpatient cardiac monitors.

Results Out of 62 PCR confirmed COVID-19 patients (34% female; mean age 67), 58 patients (93.5%) received both HC and AZ, while 4 patients (6.5%) received HC alone. Hypertension was the most common co-morbidity (33.5%) followed by diabetes mellitus (16%), known ischaemic heart disease (19.4%) and atrial fibrillation (8%). Twenty-three patients (37.1%) were on ≥2 additional QT prolonging medications. Mean baseline QTc was 445.7 msec (SD 30.4). The mean QT peak was 469.3 msec (SD 44.5) with a mean change in QTc of 28.4 msec (SD 31.4). QT prolongation was seen in 62.9% of patients, with increase in QTc ≥60 msec or QT peak ≥500 msec in 24.2% of patients. The mean length of stay was 19.7 days (SD 15.2) (range 3–57 days). Treatment was stopped in 6 patients (9.7%) due to QT prolongation. There were no cases of torsade de pointes (TdP). Mortality was 22.6%, with 16.1% of patients admitted to an intensive care unit (ICU). Patients with QT prolongation had a significantly higher risk of death (33% vs 4.3%), with an increased likelihood of ICU admission (20.5% vs 8.7%), and increased length of stay (24.7 days vs 18.6 days).

Conclusions In this study, patients who were treated with HC and AZ were at high risk of QT prolongation. QT prolongation was associated with higher mortality, increased ICU admission and longer length of stay. Close cardiac monitoring and rationalisation of additional QT prolonging drugs are essential to prevent adverse cardiac events with this treatment regimen.

2 A HIERARCHICAL ANALYSIS OF ELIGIBILITY FOR PCSK9 INHIBITION IN IRELAND: BRIDGING THE DIVIDE BETWEEN THE NCPE MANAGED ACCESS PROTOCOL AND ESC/EAS GUIDELINES

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Introduction In 2019, the national center for pharmaco-economics (NCPE) released a managed access protocol (MAP) for the prescribing of proprotein convertase subtilisin/kexin type 9 inhibitors (PCSK9i) in Ireland. To be eligible for a PCSK9i, patients must have had a myocardial infarction or coronary artery bypass grafting, LDL of >4.0 mmol/L, treated with high dose statin and ezetimibe. In contrast, the 2019 ESC/EAS guidelines on the management of dyslipidaemias recommend that patients at ‘very high risk’ with an LDL-C of >1.4 mmol/L on a maximally tolerated dose of a statin and ezetimibe, be considered for PCSK9i. We aimed to define the proportion of patients who are suitable for a PCSK9i following completion of cardiac rehabilitation based on these criteria.

Method We retrospectively analysed data on patients undergoing cardiac rehabilitation in our center from January 2018 to December 2019. We then applied the NCPE MAP and the ESC/EAS criteria to assess eligibility for a PCSK9i in the cohort. ‘Very high risk’ was defined as documented atherosclerotic coronary artery disease as per ESC dyslipidaemias guidelines.

Results The analysis includes 299 patients, who had complete lipid profiles at baseline and 6 months of follow-up, and who have a history of coronary artery disease. Baseline characteristics, mean age 62.5 years, 76% male. 202 (67.6%) patients had a history of MI or CABG making them eligible for a PCSK9i based on NCPE clinical criteria. Only 1 patient (0.5%) in this group was on a high dose statin, ezetimibe and had a 6 month LDL-C of >4.0 mmol/L making them eligible for a PCSK9i as per NCPE MAP criteria. In contrast to the NCPE MAP criteria all 299 patients were deemed eligible for a PCSK9i based on ESC/EAS clinical criteria of ‘very high risk’. 160 patients (53.5%) had an LDL-C level >1.4 mmol/L at 6 months despite maximally tolerated statin therapy, mean LDL-C 2.29 mmol/L. Only a minority of patients in this cohort were on ezetimibe, 30/160 (18.7%), however previous studies have shown that on average ezetimibe reduces LDL-C by 25% in combination with statins. Based on this, we sought to define the cohort who would potentially be eligible if they had been on ezetimibe and experienced a 25% reduction in LDL-C. 81/160 patients had a higher risk of death (33% vs 4.3%), with an increased likelihood of ICU admission (20.5% vs 8.7%), and increased length of stay (24.7 days vs 18.6 days).

Conclusions In this study, patients who were treated with HC and AZ were at high risk of QT prolongation. QT prolongation was associated with higher mortality, increased ICU admission and longer length of stay. Close cardiac monitoring and rationalisation of additional QT prolonging drugs are essential to prevent adverse cardiac events with this treatment regimen.