AHA COVID-19 Clinical Guidance Series
Considerations for Drug Interactions on QTc in Exploratory COVID-19

CREATIVE BRIEF

BRAND STATEMENT: The American Heart Association is deeply concerned about the public health crisis facing our world. Our top priority regarding coronavirus (COVID-19) is the health and well-being of individuals and their families today and in the future, in every community, everywhere.
Our mission – to be a relentless force for a world of healthier, longer lives – is more important than ever.

PROJECT BACKGROUND: The American Heart Association is creating a series of podcasts to reach healthcare providers who need critical information to provide care for cardiovascular and cerebrovascular patients who require acute care services within the context of the COVID-19 pandemic in the United States as well as inform urgent clinical care practices within in other countries.

TARGET AUDIENCE: All healthcare providers need to be aware of medications which have been identified to prolong the QT interval. Others who may also be interested in, and impacted by this content, including healthcare administrators, policy makers, scientists and the general public.

OBJECTIVE: To share current information with healthcare providers regarding proarrhythmia effects of hydroxychloroquine and azithromycin which may be used in the treatment of COVID-19.

KEY CONSUMER BENEFIT: Sharing of information can hopefully improve clinical care and lessen the impact of COVID-19 by those who listen to this program.

TONE: Urgent, Inclusive, Empathetic, Informative, Welcoming

KEY ON-AIR CONTRIBUTORS:

HOST:

Mariell Jessup, MD, FAHA Chief Science and Medical Officer American Heart Association Dallas, Texas

EXPERT

Dan M. Roden, M.D.C.M. Senior Vice President for Personalized Medicine Interim Division Chief, Division of Cardiovascular Medicine Clinical Cardiac Electrophysiology Program Faculty Vanderbilt University Nashville, TN

RUN OF SHOW

SHOW OPEN (3 MIN)

Welcome to our American Heart Association Podcast discussing Considerations for Drug Interactions on QTc in Exploratory COVID-19

Mariell introduces herself.

GUEST INTRO (30 SEC)
I'm very excited to have Dr. Dan Roden join me today

Dr. Roden is Senior Vice President for Personalized Medicine
Interim Division Chief, Division of Cardiovascular Medicine
Clinical Cardiac Electrophysiology Program Faculty
Vanderbilt University in Nashville, TN

Welcome to the podcast Dr. Roden

Q &A (15 min)

1. How does your community decide that a drug causes TdP (Torsades de Pointes)?

Databases, in vitro, case reports. Crediblemeds.org website. I think it is fair to say that while he in vitro, clinical and epidemiologic data all show that both HCQ and azithromycin can provoke arrhythmias, the risk ordinarily seems small – nothing like sotalol or dofetilide or methadone. But what we don't know is what happens in the patient with covid-19.

2. What do clinicians do to identify patients at risk?

Certain risk factors are well known … female sex, hypokalemia, Underlying heart disease, recent conversion from AF. long baseline QT including patients with the congenital long QT syndrome. Cutoff not well described but 500 msec seems reasonable for QTc.

3. Is there something special about the COVID-19 patient?

No real data yet, but causes for concern: Hypokalemia may be common in the ICU. There's some evidence that systemic inflammation can prolong QT. Fever is well known to make some genetic arrhythmia syndromes worse and there is a bit of data that fever may also prolong QT.

4. If drugs with TdP potential must be given, how should they best be monitored?

Ideally with an ECG at baseline and then at the time of expected peak QT, often around a2 hours after a dose. If the QTc gets above 500, the drug should be stopped. ECG monitoring may not be feasible in covid-19 patents. So, the best option may be to find patents at risk before they start by looking at baseline QTc duration. There are also certain QT patterns like a bifid T wave that may add to concern.

5. If a drug or drug combination is felt to have caused TdP-what should be done next? Is stopping the drug(s) enough?

Sometimes it is impossible to be sure which drug in a poly-drug regimen is the culprit and there may be more than one. The usual advice is to stop them all – may not be possible. Get the K close to 5. Give empiric Mg. If episodes of TdP are recurrent, give more Mg. then the usual – iso, pacing etc. complicated in this setting).

6. Is there anything specific about the combination of azithromycin and hydroxychloroquine that warrants concern? Are the drugs given individually risky?

Combinations of QT prolonging drugs are usually thought to have additive effects. Interestingly, there are in vitro data that these two drugs may provoke arrhythmias not by typical QT prolonging mechanisms. What we don't have are any data on the effects of this combination in cellular systems or in the normal or stressed or diseased human heart.

7. Anything else clinicians should know?

We are in an entirely new therapeutic space, so not only are we searching for efficacy, we also have to be vigilant about side effects especially ones that haven't been described before. There is lots of understandable enthusiasm for trying whatever might work, but we'll never know if anything works unless we use reasonable controls. That applies to efficacy as well as to side effects.

Calls-to-Action

What action or key takeaways would we like to leave with our audience?

We're in uncharted territory, but we do have a wealth of prior experience and knowledge to minimize risk of this particular adverse drug event.

Closing Thoughts

Please return online to AHA Professional Heart Daily for additional podcasts planned for this series to include COVID-19 in diabetics, pulmonary hypertension and other concurrent cardiovascular diseases.