PSNet
PATIENT SAFETY NETWORK

Cardiac Arrest in a Woman with UTI: A Case of QT Prolongation

November 27, 2019
Kulig CE, Ebong IA. Cardiac Arrest in a Woman with UTI: A Case of QT Prolongation. PSNet [internet]. 2019.
https://psnet.ahrq.gov/web-mm/cardiac-arrest-woman-uti-case-qt-prolongation

The Case

A 36-year-old woman with a history of depression, bipolar disorder and a recent manic episode requiring inpatient psychiatric hospitalization presented with complaints of abdominal pain, decreased appetite, nausea, and generalized weakness. On admission, she was found to have a urinary tract infection and was started on intravenous levofloxacin. She was severely volume depleted and received intravenous hydration, including her home medications, which included quetiapine, an atypical antipsychotic and lithium for her bipolar disease. She also received multiple doses of intravenous ondansetron and metoclopramide as treatment for nausea.

Eighteen hours after admission, she was observed to be bradycardic with a widening QRS complex on telemetry. On bedside evaluation, the patient was found to be unresponsive and pulseless; cardiopulmonary resuscitation was initiated. A quick chart review revealed that the patient was receiving her multiple antipsychotic medications, intravenous levofloxacin and several doses of ondansetron and metoclopramide. She was resuscitated according to the advanced cardiac life support protocol and received intravenous calcium, magnesium and sodium bicarbonate. She achieved return of spontaneous circulation. At that time, her electrocardiogram showed a prolonged QT interval of 610 msec, which was attributed by the clinical team to concomitant use of multiple QT-prolonging medications. No electrocardiogram had been obtained at the time of admission, so the patient's QT interval on antipsychotic medications alone could not be ascertained.

The Commentary

By Caitlin E. Kulig, PharmD and Imo A. Ebong, MBBS, MS

This case highlights how commonly prescribed medications can lead to serious adverse events when used in combination, even when the same medications might be well tolerated when used alone. Specifically, the

concurrent use of multiple QT prolonging medications resulted in severe QTc prolongation and clinical torsades de pointes.

Torsades de pointes is a variant of polymorphic ventricular tachycardia in which the ventricular rate is faster than 100 beats per minute with associated variations in the QRS axis or morphology. It is a cause of ventricular fibrillation. The risk factors for drug-induced QT prolongation include age, bradycardia, left ventricular failure, electrolyte abnormalities including hypokalemia and hypomagnesemia, hepatic dysfunction, congenital long QT syndrome, and recent cardioversion.[1,2] The female sex has also been identified as a risk factor in prior studies and rate-corrected QT (QTc) intervals average 20 milliseconds longer in women when compared to men.[1,2] The response to QT-prolonging medications is also greater in women than men.[3,4] The QTc refers to a QT interval that has been corrected for the patient's heart rate and is readily determined from online calculators.

Fluoroquinolones have been repeatedly associated with prolonged QT interval and torsades de pointes, especially gatifloxacin and levofloxacin, which are commonly used for treating community-acquired pneumonia and urinary tract infection.[5-8] Previous studies have shown that fluoroquinolones block expression of the *HERG* gene, which leads to inhibition of the delayed rectifier potassium channel resulting in delayed repolarization.[9,10] The frequency of torsades de pointes associated with taking levofloxacin is estimated to be 5.4 cases for every 10 million prescriptions.[6] The overall risk is low, but it increases significantly in the presence of other risk factors and concurrent use of other medications that prolong the QT interval.[6] Along with intravenous levofloxacin, the patient in this case was receiving medications for her bipolar disease including quetiapine and lithium as well as ondansetron and metoclopramide, all of which can independently increase the QTc.[11] Although the patient was successfully resuscitated, she did experience a cardiac arrest that could have been fatal.

Approach to Improving Safety

Many of the medications involved in this case, such as ondansetron and metoclopramide, are commonly used in seriously ill patients. Therefore, a thorough review of the patient's medication list to identify potential drug-drug interactions should have occurred before new medications were prescribed. In this case, alternative agents that do not affect the QT interval should have been considered for the treatment of her urinary tract infection and nausea. And because the patient was receiving multiple QT-prolonging medications, an electrocardiogram should have been obtained on admission, particularly since new QT-prolonging medications were to be added to her regimen.

Pharmacy and nursing staff should play active roles to ensure that orders placed by prescribers are thoroughly reviewed before medications are administered to the patient. In this case, pharmacy repeatedly verified the prescribed medications without checking for potential interactions between the various medications that the patient was receiving. Policies that enhance these safety checks could prevent adverse events by engaging nurses, physicians and pharmacists in identifying problematic combinations of medications in a timely manner. Additionally, the list of drugs that are known to prolong the QTc interval should be readily available to prescribers. The pharmacy department should regularly review and update this list as part of its patient safety efforts. A list of QTc prolonging medications is available online at: https://crediblemeds.org/healthcare-providers

Since most US hospitals have implemented computerized physician order entry systems with clinical decision support tools, alerts should prompt prescribers to check baseline and/or repeat electrocardiogram results when QT prolonging medications are ordered. Unfortunately, “alert fatigue” often leads prescribers to ignore these prompts.[12] Given that torsades de pointes is an especially serious adverse event, QT-related alerts should be more prominent or more difficult to ignore than alerts related to more benign side effects. Pharmacists can help prescribers to identify safer alternatives to medications known to cause prolonged QT intervals.

Drug-drug interactions are common, but some are especially dangerous and increase patients’ risk for significant adverse events, such as the one experienced in this case. Health care systems need to implement checks that prevent these types of errors and ensure that their staff are educated and empowered to decrease the risk of adverse drug reactions. The error in this case was only recognized after the patient suffered a cardiac arrest. Luckily, QTc prolongation was immediately rectified with a good overall outcome, thanks to the early post-arrest recognition of the pharmacologic problem. To prevent other cases like this one, health care organizations need to put systems in place to ensure that their staffs are educated and know how to avoid these types of incidents.

Take Home/Teaching Points

- Patient medications, both prior-to-admission and after hospitalization, should be reviewed for the presence of potential drug-drug and drug-disease interactions before new orders are placed.
- In patients who are already receiving QTc prolonging medications, an electrocardiogram should be obtained on admission to serve as a baseline; additional electrocardiograms should be obtained if indicated.
- If a potential new medication is also known to cause QTc prolongation, alternative agents should be considered. The optimal time to re-check the electrocardiogram is at peak concentrations of the QTc prolonging agents.
- If multiple agents are used, consider checking the electrocardiogram at the peak concentration of the most offending agent. Careful attention should be taken to keep magnesium and potassium levels within the appropriate range by adequate supplementation as needed.
- Prescribers and others on the healthcare team should be aware of medications associated with a high risk of causing QTc prolongation and recognize that the risk of torsades de pointes increases with the use of each additional QTc-prolonging agent, especially when the patient has other risk factors.
- It is important that every member of the health care team be actively involved in the medication review process especially when new medications are prescribed. The addition of a clinical pharmacist making daily rounds with the team may be helpful.
- For high-risk QT prolonging medications (e.g. IV levofloxacin, IV haloperidol, etc.), the electronic medical record can be programmed to send best practice prompts to alert the provider and healthcare team of the increased risk of QTc prolongation and torsades de pointes.

Caitlin E. Kulig, PharmD
PGY-2 Cardiology Pharmacy Resident
Department of Pharmacy Services
University of California, Davis

Imo A. Ebong, MBBS, MS
Assistant Clinical Professor
Department of Cardiovascular Medicine
University of California, Davis

References

1. Roden DM. Drug-induced prolongation of the QT interval. *N Engl J Med* . 2004;350:1013-1022.

2. Yap YG, Camm AJ. Drug induced QT prolongation and torsades de pointes. *Heart*. 2003;89:1363-1372.

3. Makkar RR, Fromm BS, Steinman RT, et al. Female gender as a risk factor for torsades de pointes associated with cardiovascular drugs. *JAMA*. 1993; 270: 2590-2597. [go to PubMed]

4. Bednar MM, Harrigan EP, Ruskin JN. Torsades de pointes associated with nonantiarrhythmic drugs and observations on gender and QTc. *Am J Cardiol*. 2002; 89: 1316-1319. [Available at]

5. Yap YG, Camm AJ. Drug induced QT prolongation and torsades de pointes. Heart. 2003;89:1363-1372.

6. Frothingham R. Rates of torsades de pointes associated with ciprofloxacin, ofloxacin, levofloxacin, gatifloxacin, and moxifloxacin. Pharmacotherapy. 2001; 21: 1468-1472.

7. Amankwa K, Krishnan SC, Tisdale JE. Torsades de pointes associated with fluoroquinolones: importance of concomitant risk factors. Clin Pharmacol Ther. 2004; 75:242-247.

8. Gandhi PJ, Menezes PA, Vu HT, et al. Fluconazole- and levofloxacin-induced torsades de pointes in an intensive care unit patient [published correction appears in Am J Health Syst Pharm. 2004; 61: 141]. Am J Health Syst Pharm. 2003; 60:2479-2483.

9. Wolbrette DL. Risk of proarrhythmia with class III antiarrhythmic agents: sex-based differences and other issues. *Am J Cardiol*. 2003; 91 (suppl): 39D-44D.

10. Kang J, Wang L, Chen XL, et al. Interactions of a series of fluoroquinolone antibacterial drugs with the human cardiac K+ channel *HERG*. *Mol Pharmacol*. 2001; 59: 122-126. [go to PubMed]

11. Thomas S, Behr E. Pharmacological treatment of acquired QT prolongation and torsades de pointes. *Br J Clin Pharmacol.* 2016; 81(3): 420-427. [go to PubMed]

12. Patient Safety Primer: Alert Fatigue. *Patient Safety Network* 2019. Accessed November 15, 2019. [Available at]

This project was funded under contract number 75Q80119C00004 from the Agency for Healthcare Research and Quality (AHRQ), U.S. Department of Health and Human Services. The authors are solely responsible for this report's contents, findings, and conclusions, which do not necessarily represent the views of AHRQ. Readers should not interpret any statement in this report as an official position of AHRQ or of the U.S. Department of Health and Human Services. None of the authors has any affiliation or financial involvement that conflicts with the material presented in this report. View AHRQ Disclaimers