Drug-Induced QTc Prolongation in Acute Care Pharmacy

Kelly Murray, PharmD, BCACP
Clinical Assistant Professor of Clinical Pharmacy
OSU-CHS, Dept. of Emergency Medicine // September 2018

Financial Disclosures

▪ None
Assessment Questions

1. Which antibiotic class is most well-known for its QTc-prolonging potential?
   A. Beta-lactams
   B. Carbapenems
   C. Tetracyclines
   D. Fluoroquinolones

Assessment Questions

2. What is the maximum single dose of ondansetron recommended to help avoid QTc-prolongation?
   A. 4 mg
   B. 8 mg
   C. 16 mg
   D. 32 mg
Assessment Questions

3. Which of the following is a scale that can be used to help determine the risk of QT prolongation in a hospitalized patient?

A. Mayfield Risk Calculation
B. Tisdale Risk Score
C. Switzer Risk Scale
D. Sims Risk Calculation

Objectives

- Identify patients at risk for prolonged QT interval based on home medication history.

- List antibiotics most associated with a prolonged QT interval.

- Select anti-nausea medications least likely to prolong the QT interval.
Overview

- QTc prolongation
  - Risk factors for Long QT Syndrome

- Medications and classes
  - General overview
  - Notable medications
  - Anti-nausea agents
  - Antibiotics

QT Prolongation
**QT Length**

- Normal QT = <440 ms
  - Prolonged QT = >500 msec // >460 msec // >450 msec
  - Varies in literature

- Incidence of QT prolongation estimated to be 35% of ED patients
  - Nearly half of these patients were discharged

- AZCERT “Known Risk” medications study =
  - 485 msec (men), 469 msec (women)

---

**Correcting a QT Interval**

- Adjusts for the patient’s heart rate

---

Single-lead electrocardiogram (ECG) showing a prolonged QT interval

The corrected QT interval (QTc) is calculated by dividing the QT interval (0.60 seconds) by the square root of the preceding RR interval (0.92 seconds). In this case, the QTc is 0.625 seconds.

https://www.uptodate.com/contents/image?topicKey=1043&imageKey=CARD%2F77018&source=outline_link&search=qt%20prolongation
QT Prolongation

- Delayed ventricular repolarization, usually manifested in prolongation of phase 2, action potential plateau phase

Risk Factors for QT Prolongation

- Females
- Elderly
- Electrolyte disturbances (hypokalemia, hypomagnesemia)
- Congestive heart failure, cardiac abnormalities
- Drug interactions
- Co-administered QT-prolonging medications
- Baseline QT prolongation

Why can QT prolongation happen?

1. Effects on ion channels

2. Genetic involvement
   - Congenital long-QT syndrome (CLQTS)

3. Medications
   - Changes to medications
   - Drug interactions
   - Cumulative effects of multiple QT-prolonging medications


What is Torsades de Pointes (TdP)?

- Rare polymorphic ventricular arrhythmia
- Occurs in self-limiting bursts
- Symptoms: dizziness, palpitations, syncope, seizures
- Can progress to ventricular fibrillation and sudden cardiac death

ECG Waveform of TdP

- Rapid, irregular QRS complexes “twisting” around the isoelectric baseline


Tisdale QTc Prolongation Risk Score

Prospective, Observational
Cardiac ICU
n= 900 (development)
n= 300 (validation)

QTc prolongation=
- >500 msec or
- increase ≥ 60 msec from baseline

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥ 68 years</td>
<td>1</td>
</tr>
<tr>
<td>Female</td>
<td>1</td>
</tr>
<tr>
<td>Loop diuretic</td>
<td>1</td>
</tr>
<tr>
<td>Serum K+ ≤ 3.5 mEq/L</td>
<td>2</td>
</tr>
<tr>
<td>Admitting QTc interval ≥ 450 msec</td>
<td>2</td>
</tr>
<tr>
<td>Acute myocardial infarction</td>
<td>2</td>
</tr>
<tr>
<td>Sepsis</td>
<td>3</td>
</tr>
<tr>
<td>Heart Failure with reduced EF</td>
<td>3</td>
</tr>
<tr>
<td>One QTc-prolonging drug</td>
<td>3</td>
</tr>
<tr>
<td>Two or more QTc-prolonging drugs</td>
<td>3</td>
</tr>
<tr>
<td>Maximum score</td>
<td>21</td>
</tr>
</tbody>
</table>

Tisdale Risk Score

<table>
<thead>
<tr>
<th>Risk Category</th>
<th>Scoring</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>High Risk</td>
<td>≥ 11</td>
<td>74%</td>
<td>77%</td>
<td>79%</td>
<td>76%</td>
</tr>
<tr>
<td>Moderate Risk</td>
<td>7-10</td>
<td>67%</td>
<td>88%</td>
<td>55%</td>
<td>88%</td>
</tr>
<tr>
<td>Low Risk</td>
<td>&lt; 7</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
</tbody>
</table>

- Identifies patients at high risk of QTc interval prolongation before developing it


Goal

- Prevent or minimize QT prolongation
- Avoid Torsades de Pointes (TdP) and sudden cardiac death
- Avoid codes

Drugs that Prolong QT and/or Cause TdP

Goals of Proarrhythmic Cardiac Safety

1. Need to determine whether a new drug has a proarrhythmic propensity

2. Implement risk management strategies and optimally safe therapeutic use of drugs known to have proarrhythmic liability

Drug Marketing Withdrawals due to Proarrhythmic Concerns

<table>
<thead>
<tr>
<th>Drug</th>
<th>Indication</th>
<th>Year Withdrawn</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prenylamine</td>
<td>Antianginal</td>
<td>1989 (UK)</td>
</tr>
<tr>
<td>Terodiline</td>
<td>Urinary incontinence</td>
<td>1991 (UK, US)</td>
</tr>
<tr>
<td>Sparfloxacin</td>
<td>Antibiotic</td>
<td>1996 (US)</td>
</tr>
<tr>
<td>Sertindole</td>
<td>Antipsychotic</td>
<td>1998 (UK)</td>
</tr>
<tr>
<td><strong>Terfenadine</strong></td>
<td><strong>Antihistamine</strong></td>
<td><strong>1998 (US)</strong></td>
</tr>
<tr>
<td>Astemizole</td>
<td>Antihistamine</td>
<td>1999 (US)</td>
</tr>
<tr>
<td>Grepafloxacin</td>
<td>Antibiotic</td>
<td>1999 (UK, US)</td>
</tr>
<tr>
<td>Cisapride</td>
<td>Gastroesophageal reflux</td>
<td>2000 (UK, US)</td>
</tr>
<tr>
<td>Levacetylmethadol</td>
<td>Opiate addiction</td>
<td>2003 (UK)</td>
</tr>
</tbody>
</table>


Thorough QT (TQT) Studies

- Phase 2 of FDA Approval
- Healthy individuals, crossover design study
  - 4 treatment arms, randomized
    1. Positive control arm, drug with known QTc prolongation (5 msec minimum comparator)
    2. Placebo
    3. Max recommended therapeutic dose of drug
    4. Supratherapeutic dose of drug

Adverse Drug Event Casualty Analysis (ADECA)

- Categories of certainty

- **KR =** [Known Risk of TdP]
- **PR =** [Possible Risk of TdP]
- **CR =** [Conditional Risk of TdP]
- **CLQT =** [Drugs to Avoid in Congenital Long QT]

https://crediblemeds.org/new-drug-list/

Most Potent QT-Prolonging Medications

- **Antiarrhythmic agents**
  - Ia - Quinidine*
  - III - Amiodarone
  - III - Dofetilide
  - III - Sotalol

*most torsadogenic potential

Dipiro 2008.
### QT Prolonging Medication Classes

<table>
<thead>
<tr>
<th>Class</th>
<th>Risk</th>
<th>Medications most likely...</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antihistamines</td>
<td>📝</td>
<td>Hydroxyzine, diphenhydramine</td>
</tr>
<tr>
<td>Antipsychotics</td>
<td>💣</td>
<td>Haloperidol, droperidol</td>
</tr>
<tr>
<td></td>
<td>🌟</td>
<td>Aripiprazole, asenapine, clozapine, iloperidone, risperidone</td>
</tr>
<tr>
<td></td>
<td>🌟</td>
<td>Olanzapine, quetiapine, ziprasidone</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>💣</td>
<td>Citalopram, escitalopram</td>
</tr>
<tr>
<td></td>
<td>💟</td>
<td>Clomipramine desipramine, imipramine, mirtazapine, nortriptyline, venlafaxine</td>
</tr>
<tr>
<td></td>
<td>💟</td>
<td>Fluoxetine, fluvoxamine, paroxetine, sertraline, trazadone, amitriptyline, doxepin</td>
</tr>
</tbody>
</table>

## QT Prolonging Medication Classes

<table>
<thead>
<tr>
<th>Class</th>
<th>Risk</th>
<th>Medications most likely…</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain medications</td>
<td>⚠️</td>
<td>Methadone, propofol</td>
</tr>
<tr>
<td></td>
<td>⚠️</td>
<td>Hydrocodone ER, buprenorphine</td>
</tr>
<tr>
<td>Acid suppressants</td>
<td>⚠️</td>
<td>Famotidine</td>
</tr>
<tr>
<td></td>
<td>⚠️</td>
<td>Omeprazole, esomeprazole, lansoprazole, pantoprazole</td>
</tr>
<tr>
<td>Antifungals</td>
<td>⚠️</td>
<td>Fluconazole, ketoconazole</td>
</tr>
<tr>
<td></td>
<td>⚠️</td>
<td>amphotericin B</td>
</tr>
</tbody>
</table>

www.CredibleMeds.org

## QT Prolonging Medication Classes

<table>
<thead>
<tr>
<th>Class</th>
<th>Risk</th>
<th>Medications most likely…</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-nausea</td>
<td>⚠️</td>
<td>Droperidol, ondansetron, chlorpromazine</td>
</tr>
<tr>
<td></td>
<td>⚠️</td>
<td>Granisetron, promethazine, prochlorperazine</td>
</tr>
<tr>
<td></td>
<td>⚠️</td>
<td>Metoclopramide</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>⚠️</td>
<td>Azithromycin, clarithromycin, erythromycin, ciprofloxacin, levofoxacin, moxifloxacin</td>
</tr>
<tr>
<td></td>
<td>⚠️</td>
<td>Gemifloxacin, telavancin</td>
</tr>
<tr>
<td></td>
<td>⚠️</td>
<td>Metronidazole</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>⚠️</td>
<td>Cocaine</td>
</tr>
<tr>
<td></td>
<td>⚠️</td>
<td>Loperamide</td>
</tr>
</tbody>
</table>

www.CredibleMeds.org
Other Notable Medications

**COCAIN**
Acts like a class I antiarrhythmic agent
- Produces local anesthetic effects via sodium channel blockade in the heart
- Alters repolarization with QT prolongation (among other things)
- Rhythm disturbances typically disappear when drug is metabolized


**LOPERAMIDE**
- Loperamide-induced cardiac toxicity
  - Excessive dose
  - Impaired drug elimination
- Present with QT prolongation, QRS widening, and ventricular dysrhythmias +/- conventional opioid toxicity symptoms

Patient Case

- A 31 year old male presents complaining of chest pain and shortness of breath. (+) for nausea/vomiting. Only medications given en route were aspirin, nitroglycerin, and ondansetron.

- **PMH**: major depressive disorder, HTN, dyslipidemia.

- **Current meds**: citalopram, lisinopril, atorvastatin.

- **NKDA**
Patient Case

- Focus should be on his cardiac workup.
  - EKG ordered. QTc = 513 msec.
  - Still need to address his nausea/vomiting.

- What do you order for nausea/vomiting?
  A. Ondansetron
  B. Haloperidol
  C. Promethazine
  D. Metoclopramide
  E. Prochlorperazine

Anti-nausea Medications

- Ondansetron ➔ Serotonin receptor antagonist
- Promethazine
- Prochlorperazine
- Chlorpromazine
- Metoclopramide ➔ Benzamide
- Droperidol ➔ Butyrophenones
- Haloperidol

Phenothiazines
Ondansetron

- QT increase and TdP risk ARE in label
- Dose-related increase in risk

- Ondansetron IV one-time doses showed QTc changes of:
  - 32mg = 21.8 msec
  - 8mg = 7.4 msec


“…no increased incidence of a patient developing a cardiac arrhythmia after a single oral dose of ondansetron.”

= no need for routine EKG and electrolyte screening in those without known risk factors

Intravenous Ondansetron and the QT Interval in Adult Emergency Department Patients: An Observational Study

Peter M. Moffett, MD, Laquisha Cartwright, PharmD, Elizabeth A. Grossart, MD, Dustin O’Keefe, MD, and Christopher S. Kang, MD

STUDY DESIGN:

n=22
(Mean 32y, otherwise healthy)

Baseline EKG

Ondansetron 4mg IV x 1 dose

EKG every 2 min x 20 min

PRIMARY OUTCOME: Mean Maximal Prolongation of QTc

<table>
<thead>
<tr>
<th>Interval length</th>
<th>Baseline QTc</th>
<th>Max QT</th>
<th>Max QTc Prolongation</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>395 (386-404)</td>
<td>415 (405-425)</td>
<td>20 (14.0-26)</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
</tbody>
</table>


Thorough QT Study Results

- Ondansetron single dose vs. moxifloxacin
- Maximum mean difference of:
  - 8 mg IV dose = 10 msec
  - 32 mg IV dose = 20 msec

Ondansetron Recommendations

- Avoid:
  - High doses (max 16mg in a single dose)
  - In patients with Congenital LQTS

- Monitor EKG:
  - Electrolyte abnormalities (low K+ or Mg+)
  - CHF
  - Bradyarrhythmias
  - Pt is taking other QT prolonging medications
  - If multiple IV doses are given within a few hours of each other

https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/020103s035_020605s019_020781s019lbl.pdf.

Phenothiazines

- Known Risk - Thioridazine, chlorpromazine
- Possible Risk - Promethazine
- Risk not assessed - Prochlorperazine

- Thioridazine is most common culprit for QT prolongation
  - Limit dose to ≤100 mg/day

Phenothiazines

- Safest choices =
  - Prochlorperazine
  - Promethazine

- Proceed with caution


Metoclopramide

- Conditional Risk =

  - May cause TdP under certain circumstances:
    - Low serum Mg+ or K+
    - Concomitant use of QT-prolonging or TdP-causing medications

A RANDOMIZED CONTROLLED TRIAL OF INTRAVENOUS HALOPERIDOL VS. INTRAVENOUS METOCLOPRAMIDE FOR ACUTE MIGRAINE THERAPY IN THE EMERGENCY DEPARTMENT

Matthew E. Gaffigan, MD, David I. Bruner, MD, Courtney Wason, BS, Amy Pritchard, CO, and Kenneth Frumkin, MD, PhD

STUDY DESIGN:

n=33 (out of 64)

Baseline EKG

Metoclopramide 10mg IV x 1 dose

EKG before discharge (in 45%)

SECONDARY OUTCOME (Metoclopramide Data Only):

<table>
<thead>
<tr>
<th>Interval length</th>
<th>Pretreatment QTc</th>
<th>Posttreatment QTc</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>428 msec</td>
<td>440 msec</td>
<td>NS</td>
</tr>
</tbody>
</table>


Metoclopramide

- Lexi-complete:
  - “...known to cause sinus arrest (with rapid IV administration or higher doses).”
  - “...torsadogenic potential... considered to be low.”
  - More common in heart failure patients with renal impairment
  - May shorten the QT interval - ???
  - Only case reports demonstrate QT prolonging effect.

Butyrophenones: DROPERIDOL

- **Known risk – 🔴⚠️**
  - QT prolongation = why you don’t have this in your toolbox
  - Black box warning decision may stem from post-marketing data, not peer-reviewed data
  - Dose-related risk (greatest with >5mg doses)


Butyrophenones: HALOPERIDOL

- **Known risk – 🔴⚠️**
  - Great for N/V/HA in patients with psych diagnoses
  - Watch for home medications as additional risk factors
  - Give IM
    - Haloperidol lactate for ED (decanoate = long acting formulation)
    - Limit IV dose to x1
  - Get a baseline EKG and consider continuous monitoring (if baseline prolongation or ≥2mg are needed).

Anti-nausea Summary

- Haloperidol = high risk (especially IV)
- Ondansetron ~20 msec
  - Consider EKG to monitor if risk factors
- Promethazine/Prochlorperazine
  - Watch for additional risk factors and concomitant medications with QT risk
- Metoclopramide
  - Watch for additional risk factors
  - Possibly the safest?

Patient Case

- CP/N/V.
- QTc = 513 msec.

- What do you order for nausea/vomiting?
  A. Ondansetron  Known QT prolongation risk - AVOID
  B. Haloperidol  Known QT prolongation risk - AVOID
  C. Promethazine  Possible QT prolongation risk
  D. Metoclopramide  Conditional QT prolongation risk
  E. Prochlorperazine  Unknown QT prolongation risk
Patient Case

- Cardiac labs came back normal. Chest infiltrates seen on x-ray.
- Dx of community-acquired pneumonia given.
- He will be treated outpatient.

ANTIBIOTICS
"Damn. I have to stop giving the first dose of azithromycin in my office."

Image from https://emcrit.org/pulmcrit/myth-busting-azithromycin-does-not-cause-torsade-de-pointes-or-increase-mortality/

**Antibiotics**
- Azithromycin
- Clarithromycin
- Erythromycin
- Ciprofloxacin
- Levofloxacin
- Gemifloxacin
- Moxifloxacin

**Macrolides**

**Fluoroquinolones**
Macrolides

- Erythromycin, azithromycin, clarithromycin
  - Known risk of TdP
  - Two major studies conflict (among others)

Azithromycin and the Risk of Cardiovascular Death

Wayne A. Ray, Ph.D., Katherine T. Murray, M.D., Kathi Hall, B.S., Patrick G. Arbogast, Ph.D., and C. Michael Stein, M.B., Ch.B.

Use of Azithromycin and Death from Cardiovascular Causes

Henrik Svanström, M.Sc., Björn Pasternak, M.D., Ph.D., and Anders Hvid, Dr.Med.Sci.

<table>
<thead>
<tr>
<th>Population</th>
<th>Risk Ratios for Azithromycin Compared to Nonuse</th>
<th>Risk Ratios for Azithromycin Compared to B-Lactam Use</th>
<th>Overall Cardiovascular Mortality Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tennessee</td>
<td>2.88, 95% CI, 1.25-2.75</td>
<td>2.49; 95% CI, 1.38-4.50</td>
<td>85.2 deaths per 1 million azithromycin courses</td>
</tr>
</tbody>
</table>

Use of Azithromycin and Death from Cardiovascular Causes

Henrik Svanström, M.Sc., Björn Pasternak, M.D., Ph.D., and Anders Hviid, Dr.Med.Sci.

Population Risk Ratios for Azithromycin compared to Nonuse  Risk Ratios for Azithromycin Compared to B-Lactam Use  Overall Cardiovascular Mortality Rate

<table>
<thead>
<tr>
<th>Population</th>
<th>Risk Ratios for Azithromycin compared to Nonuse</th>
<th>Risk Ratios for Azithromycin Compared to B-Lactam Use</th>
<th>Overall Cardiovascular Mortality Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Denmark</td>
<td>2.85; 95% CI 1.13-7.24</td>
<td>0.93; 95% CI 0.56-1.55</td>
<td>15.4 deaths per 1 million azithromycin courses</td>
</tr>
</tbody>
</table>

NS


Ray vs Svanstrom

<table>
<thead>
<tr>
<th>Population</th>
<th>Risk Ratios for Azithromycin compared to Nonuse</th>
<th>Risk Ratios for Azithromycin Compared to B-Lactam Use</th>
<th>Overall Cardiovascular Mortality Rate</th>
<th>+ Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tennessee</td>
<td>2.88, 95% CI 1.25-2.75</td>
<td>2.49; 95% CI 1.38-4.50</td>
<td>85.2 deaths per 1 million azithromycin courses</td>
<td>+ 47</td>
</tr>
<tr>
<td>Denmark</td>
<td>2.85; 95% CI 1.13-7.24</td>
<td>0.93; 95% CI 0.56-1.55</td>
<td>15.4 deaths per 1 million azithromycin courses</td>
<td>- 1</td>
</tr>
</tbody>
</table>

The implications of these data have yet to be determined.

- Lexi-complete

Fluoroquinolones

- Most associated with gatifloxacin, moxifloxacin, and withdrawn agents sparifloxacin and grepafloxacin.

- KR – levofloxacin, ciprofloxacin, moxifloxacin
- PR - gemifloxacin


Fluoroquinolones

- Makaryus et al.
  - N=38; cipro = 11 + levofloxacin = 27
  - Ciprofloxacin = NS change in longest QT, mean QTc
  - Levofloxacin = significant increase in longest QT, but not mean

- Lapi et al.
  - n=605,127; 1838 cases of arrhythmias identified
  - FQ use + arrhythmia RR=1.76; 95% CI 1.19-2.59; new current use RR=2.23;95% CI 1.31-3.80
  - Ciprofloxacin RR=2.15
  - Levofloxacin = “did not appear to increase rate of serious arrhythmia”

Azithromycin and the Risk of Cardiovascular Death

Wayne A. Ray, Ph.D., Katherine T. Murray, M.D., Kathi Hall, B.S., Patrick G. Arbogast, Ph.D., and C. Michael Stein, M.B., Ch.B.

- Fluoroquinolone Analysis:

“…ciprofloxacin was not associated with an increased risk of cardiovascular mortality.”

“It is unclear whether or not levofloxacin was associated with an increased risk…”


- Conclusion from the Ray study:

- Azithromycin CV risk > ciprofloxacin CV risk

- Azithromycin vs levofloxacin CV risk not statistically significantly different

Use of Azithromycin and Death from Cardiovascular Causes

Henrik Svanström, M.Sc., Björn Pasternak, M.D., Ph.D., and Anders Hviid, Dr. Med. Sci.

- **Fluoroquinolone Analysis:**
  - n=909,656 courses of fluoroquinolones evaluated (ciprofloxacin = 83%)
  - NO increase in risk of serious arrhythmias with FQ vs beta-lactams


---

- **Levofloxacin can be used effectively as a positive control in thorough QT/QTc studies in healthy volunteers**
  - Jorg Taubel, Adil Naseem, Tomohiko Harada, Doolao Wang, Radivoj Arozina, Ulrike Lorch & A John Camm

- **Levofloxacin single dose 1000 mg or 1500 mg versus moxifloxacin 400 mg**

- **Prolongation Potential at 3.5 h**
  - 1000 mg = 4.42 msec (2.44-6.39 msec)
  - 1500 mg = 7.44 msec (5.47-9.42 msec)

Case Revisited

Patient Case

- Dx of community-acquired pneumonia given.
- He will be treated for CAP outpatient.

- What antibiotic plan should you recommend?
  A. Doxycycline
  B. Azithromycin
  C. Levofloxacin
  D. Beta lactam + doxycycline
  E. Levofloxacin + doxycycline
Patient Case

- Dx of community-acquired pneumonia given.
- He will be treated for CAP outpatient.

- What antibiotic plan should you recommend?
  A. Doxycycline
  B. Azithromycin
  C. Levofloxacin
  D. Beta lactam + doxycycline
  E. Levofloxacin + doxycycline
Plan of Action for Pharmacists

Review those medication lists…

- Recommend medications that don’t pose risk of prolonging QT (if possible)
Advocate for calculating risk scores…

- Tisdale Risk Score is one option

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥ 68 years</td>
<td>1</td>
</tr>
<tr>
<td>Female</td>
<td>1</td>
</tr>
<tr>
<td>Loop diuretic</td>
<td>1</td>
</tr>
<tr>
<td>Serum K+ ≤ 3.5 mEq/L</td>
<td>2</td>
</tr>
<tr>
<td>Admitting QTc interval ≥ 450 msec</td>
<td>2</td>
</tr>
<tr>
<td>Acute myocardial infarction</td>
<td>2</td>
</tr>
<tr>
<td>Sepsis</td>
<td>3</td>
</tr>
<tr>
<td>Heart Failure with reduced EF</td>
<td>3</td>
</tr>
<tr>
<td>One QTc-prolonging drug</td>
<td>3</td>
</tr>
<tr>
<td>Two or more QTc-prolonging drugs</td>
<td>3</td>
</tr>
<tr>
<td>Maximum score</td>
<td>21</td>
</tr>
</tbody>
</table>

Watch for drug interactions and multiple QTc-prolonging meds…

- Amiodarone + fluoroquinolones
  - Increased risk of TdP/QT prolongation
  - Concomitant blockade of cardiac potassium channels

- CYP450 inhibitors vs substrates
  - 1A2 – haloperidol increased when amiodarone, ciprofloxacinc, or fluvoxamine given
  - 2D6 – haloperidol, promethazine, prochlorperazine, SSRIIs increased when given with amiodarone
  - 3A4 – amiodarone, methadone, TCAs increased with azole antifungals, metronidazole, diltiazem
Nausea

- Don’t need to get an EKG on everyone
  - Only those with RFs
- Recommend haloperidol IM
- Consider EKG when redosing ondansetron
- Use metoclopramide if prolonged QT at baseline or if at risk for drug-induced QT prolongation
  - Alternate option = promethazine

Antibiotics

- Avoid QT prolonging antibiotics if possible
  - Options for atypical and respiratory coverage exist
    - Outpatient: doxycycline
    - Inpatient: doxycycline, tobramycin, gentamicin

- Get baseline EKG if your options are limited
Final Thoughts

- Read primary literature to form your own conclusions
  - Clinical relevance may be lacking
  - FDA recommendations, warnings exist
- Avoid unnecessary risk when possible
- Use caution when ordering and prescribing

But just in case…
Resources

  - Accounts are free.
  - There’s an app for that.

Assessment Questions

1. Which antibiotic class is most well-known for its QTc-prolonging potential?

   A. Beta-lactams
   B. Carbapenems
   C. Tetracyclines
   D. Fluoroquinolones

   [Correct answer: D. Fluoroquinolones]
Assessment Questions

2. What is the maximum single dose of ondansetron recommended to help avoid QTc-prolongation?
   
   A. 4 mg  
   B. 8 mg  
   C. 16 mg  
   D. 32 mg

Assessment Questions

3. Which of the following is a scale that can be used to help determine the risk of QT prolongation in a hospitalized patient?
   
   A. Mayfield Risk Calculation  
   B. Tisdale Risk Score  
   C. Switzer Risk Scale  
   D. Sims Risk Calculation
References

References


Drug-Induced QTc Prolongation in Acute Care Pharmacy

Kelly Murray, PharmD, BCACP
Clinical Assistant Professor of Clinical Pharmacy
OSU-CHS, Dept. of Emergency Medicine // September 2018