Background

- Macrolides are associated with QTc prolongation and increased risk for life-threatening arrhythmias, including torsades de points (Tdp).
- Patients who received a 5-day course of azithromycin had significantly higher incidence of cardiovascular (CV) mortality as compared to those receiving other antibiotics.
- Patients at high risk for CV mortality include:
  - Pre-existing CV risk factors
  - Underlying CV disease
  - Concomitant pro-arrhythmic drugs
  - Elderly
- In March 2013, the FDA issued a drug safety communication highlighting the potential for azithromycin to cause abnormal changes in cardiac electric activities and fatal cardiac rhythms.
- Azithromycin drug labels were updated to strengthen the warning related to QTc prolongation and Tdp.
- The University of Chicago Medicine (UCM) implemented a “Drug-Induced QTc Prolongation Monitoring Guideline” in fall 2011 to optimize EKG monitoring and electrolyte replacement among inpatients receiving QTc prolonging medications.

The Intervention

- Retrospective review of azithromycin orders for adult inpatients
  - To characterize patient population receiving azithromycin
  - To determine if patients receiving azithromycin are monitored appropriately with EKGs per UCM policy
- FDA warning communicated to medical staff through email and the antimicrobial stewardship website (Mar 2013)
- Community acquired pneumonia clinical pathway and order set that encourage assessment of baseline QTc for atypical coverage (azithromycin / fluoroquinolone versus doxycycline) (Oct 2013)

Results

Table 1. Patient Demographics (N=50)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean ± SD or N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>60.4 ± 18.5</td>
</tr>
<tr>
<td>Gender (male)</td>
<td>23 (46)</td>
</tr>
<tr>
<td>Duration of Therapy (days)</td>
<td>4 ± 2</td>
</tr>
<tr>
<td>% of Patients with ≥ 1 Risk Factor for Drug-Induced QTc Prolongation</td>
<td>43 (86)</td>
</tr>
<tr>
<td># of Risk Factors</td>
<td></td>
</tr>
<tr>
<td>1 Risk Factor</td>
<td>16 (32)</td>
</tr>
<tr>
<td>2 Risk Factors</td>
<td>15 (30)</td>
</tr>
<tr>
<td>3 Risk Factors</td>
<td>8 (16)</td>
</tr>
<tr>
<td>4 Risk Factors</td>
<td>4 (8)</td>
</tr>
</tbody>
</table>

Prevalence of FDA-Identified Risk Factors

- Concomitant QTc prolonging medications (62%)
  - Voriconazole, citalopram, haloperidol, ondansetron, famotidine, tacrolimus, quinidine, procainamide, dofetilide, amiodarone, sotalol
- Elderly (46%)
- CV disease (CHD, LVH, CHF) (28%)
- Baseline QTc prolongation (≥ 470 msec) (24%)
- Uncorrected hypokalemia and hypomagnesemia (16%)

Indication for Azithromycin

- Pneumonia
- COPD Exacerbation
- Acute Chest Syndrome
- MAI
- Premature Rupture of Membrane (PROM)

Compliance with UCM Drug-Induced QTc Prolongation Monitoring Guideline

- Overall compliance rate: 25/50 (50%)
- Non-telemetry: 5/27 (19%)

Lessons Learned/Conclusions

- Azithromycin was frequently initiated in high risk patients
- Majority of patients received azithromycin for indications with clear therapeutic alternatives

Next Steps

- Continued provider education
- Assess impact of interventions on azithromycin use

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