The Importance of EKG Monitoring in Geriatric Patients at Risk of Polypharmacy-Induced QTc Prolongation

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BACKGROUND
Polypharmacy, the concurrent use of multiple drugs by a patient for one or more conditions, is rising as the population ages.1 One potential adverse event of polypharmacy is a prolonged QT interval, which reflects the duration of ventricular repolarization.1 A QT interval longer than 460 ms is an at-risk value.2 A QT interval corrected for heart rate from an electrocardiogram (EKG), holds clinical significance when prolonged because it is a risk factor for a life-threatening polymorphic ventricular tachycardia/arrhythmias called torsade de pointes. Potential risks include the Agency for Healthcare Research and Quality, 543,000 adults over the age of 65 were hospitalized for an irregular heartbeat in 2009. Most sudden cardiac deaths, “300,000 per year in the US, are caused by ventricular arrhythmias.”1

Despite these alarming statistics, it is important to note that drug-induced QT prolongation is a modifiable risk factor for TdP. Therefore, its detection/prevention via EKG monitoring and pharmacotherapy adjustments is of particular importance in geriatric patients, who exhibit a progressive QT prolongation with age.3 According to the Centers for Medicare and Medicaid Services, over 25% of patients in nursing facilities in the US receive antipsychotic (AP) medications, one of many non-cardiac classes of medications that have been identified by regulatory agencies to potentially lengthen the QT interval.

Currently, literature identifying pharmacists’ role in monitoring and reducing drug-induced QT prolongation is limited. Therefore, the goal of this research is to identify the impact pharmacists can have on reducing QT prolongation through medication review and provider suggestions. It also provides information to health care professionals about the importance of EKG monitoring practices in elderly patients with increased risk of QT prolongation.

STUDY OBJECTIVES & HYPOTHESIS
OBJECTIVE: The primary objective is to determine the impact of pharmacists on the potential reduction of cardiac complications as measured by a reduction in elevated QTc interval, for patients engaged in polypharmacy. The secondary objective is to determine the pattern or frequency of EKGs on file and pharmacists recommendations made.

Hypothesis: Most residents may not have EKG records on file. For those that have an elevated QTc interval >450 msec for which providers accepted pharmacists recommendations to either decrease, change or discontinue medication, there will be a reduction in QTc interval per follow-up EKG.

METHODS
Institutional review board approval was obtained by Western University of Health Sciences. This retrospective chart review was done at Los Angeles Jewish Home for the Aging (LAJH), a 238 bed long-term skilled nursing facility via the Achieve Matrix Software. An initial query was performed to identify all patients taking antipsychotics with any risk of QTc prolongation, 81 patients were retrieved and their records were reviewed to further identify patients who were on at least 1 antipsychotic prior to 01/01/2015 -12/31/15. Patients were excluded if no data was available or if they expired prior to 2015. Patients included met the following criteria: 1) concurrently taking ≥2 QT-prolonging medications with at least an antipsychotic. 2) ≥70 years of age. 3) had an EKG on file indicating elevated QTc >450 msec, and 4) a pharmacist recommendation present. Only 47 patients were asked to participate for the inclusion criteria to assess the primary objective, therefore a power chart review and sub-analysis was done on a total of 31 patients who were on ≥2 QTc prolonging medications, with at least 1 being an antipsychotic, and ≥70 years old. Data collected included demographics, medical comorbidities, number of EKGs on file, QTc intervals if available, and details of pharmacist recommendations and provider responses. To maintain consistency, CredibleMedical1 list was used to identify medications for which there is a known, conditional, or potential risk of QTc prolongation.

Pharmacist’s exact tests, chi-square, ANOVA and t-tests were used for statistical analysis and conducted using GraphPad Prism and Microsoft Excel. P-values were considered statistically significant at p<0.05.

RESULTS

Table 1. Characteristics and demographics of patients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>QTc &gt;450 (n=14)</th>
<th>QTc &gt;450 w/Pharmacist (n=4)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>80.1 (7)</td>
<td>80.0 (5)</td>
<td>1.01</td>
</tr>
<tr>
<td>Gender</td>
<td>4 (28.5%)</td>
<td>2 (50%)</td>
<td>0.32</td>
</tr>
<tr>
<td>African-American</td>
<td>3 (21.4%)</td>
<td>0 (0%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Hispanic</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Number of Medications</td>
<td>14 (100%)</td>
<td>4 (100%)</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Table 2. Distribution of Drugs by Risk Category

<table>
<thead>
<tr>
<th>Drug Category</th>
<th>QTc &gt;450 (n=14)</th>
<th>QTc &gt;450 w/Pharmacist (n=4)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antipsychotics</td>
<td>14 (100%)</td>
<td>4 (100%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>10 (71.4%)</td>
<td>2 (50%)</td>
<td>0.56</td>
</tr>
<tr>
<td>Anticoagulants</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Antiarrhythmic</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Antihistamines</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Antidiabetics</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Calcium channel blockers</td>
<td>2 (14.3%)</td>
<td>1 (25%)</td>
<td>0.88</td>
</tr>
<tr>
<td>Other</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Table 3. Distribution of EKG Status vs Pharmacist Recommendation Status

<table>
<thead>
<tr>
<th>EKG Status</th>
<th>QTc &gt;450 (n=14)</th>
<th>QTc &gt;450 w/Pharmacist (n=4)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Change</td>
<td>4 (28.5%)</td>
<td>2 (50%)</td>
<td>0.32</td>
</tr>
<tr>
<td>Improvement</td>
<td>10 (71.4%)</td>
<td>2 (50%)</td>
<td>0.56</td>
</tr>
</tbody>
</table>

Figure 1. Percentage of EKGS Performed on Patients Taking at least 2 or More QTc-Prolonging Medications. Nearly half of patients (55.6%) with some risk of QT prolongation from polypharmacy did not have EKG done.

Figure 2. Comparison of the average time lapsed between pharmacist recommendation and response to two pharmacists among 22 patients who were at-risk for QT prolongation. A significant difference (p<0.05) was observed between pharmacists when comparing the number of days taken to respond to pharmacist recommendation.

Figure 3. Distribution of Medication Class per Group. In general, patients who had elevated QTc intervals who were on more antipsychotics and antidepressants compared to those with normal QTc intervals and with no EKG. Patients with no EKG or those with normal QTc intervals, had less EKG done (p<0.05).

DISCUSSION

For the 4/13 patients that met the initial inclusion criteria, the primary objective to determine the effect of pharmacist recommendations measured by a decrease in QTc interval was unable to be achieved due to lack of post-recommendation follow-up EKGS on file.

The presence of coronary artery disease was found to be significantly higher in patients with elevated QTc intervals when compared between the three groups (p value >0.01). Table 1). Sub-analyses on 31 patients revealed that 86% of patients risk of QTc prolongation had no EKG on record and remained at risk (Figure 1). This provides an opportunity to develop a protocol in which pharmacists could order EKGs to monitor patients at risk.

Though sub-analysis demonstrated no significant differences in the number of recommendations accepted, not accepted, and not made between the 3 groups, it is important to note that 55.6% of the risk factors with QTc > 450 msec did not have a follow-up pharmacist recommendation (Figure 2).

There was no significant difference in distribution of medications by risk category amongst groups, further emphasizing the need to monitor patients engaged in polypharmacy (Table 1). Evidence-based literature suggests that polypharmacy is becoming common practice in elderly and can increase the risk of drug-drug interactions, supporting the need for further assessment of additional polypharmacy useful EKG monitoring prior to and after administration of drugs with anticipated QTc prolongation may be warranted.

LIMITATIONS

Small sample size limits generalizability
Narrow demographic range: 100% Caucasian population
Lack of EKG orders available, either upon admission, initiation of treatment, or follow-up
Retrospective study: some amount of data may have been missing from medical records
QTc interval as a surrogate measurement: QTc is rate-corrected and is reliable with normal T waves at physiological heart rates, but unreliable at elevated HR, abnormal T waves, and prominent U waves
A multivariate linear regression analysis was not performed
Potentially undetected HERG mutation: HERG mutation, a risk factor for QTc prolongation, was not completed
Indication of medications did not always correlate to an ICD 9/10 diagnosis

CONCLUSION

EKGs are an easily accessible monitoring tool for QTc interval prolongation and are utilized in the elderly population. The findings in this study suggest the consideration of a new protocol under which pharmacists can order EKGs for medication monitoring purposes to maximize patient safety. Though the American Society of Consultant Pharmacists reports that there has been a 27% reduction in antipsychotic use in nursing home residents and that the national prevalence of antipsychotic medication use is down 17.4% of the third quarter of 2015, in general, polypharmacy is still on the rise. For this reason, the concern may provide QTc prolonging medications leading to increased risk of TdP remains. Increased awareness of potential complications can allow pharmacists and potentially prevent prevent and monitor elderly patients at risk of polypharmacy-induced QTc prolongation.

REFERENCES & ACKNOWLEDGMENTS

1. Masoodi, N. Polypharmacy: To Err is Human, To Correct is Divine. BJMP 2008;1(1): 6-9
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ACKNOWLEDGEMENTS

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NOTES

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