Evaluation of Sotalol Prescribing Practices in Adult Populations

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Introduction

Purpose

Sotalol is a cardiac antiarrhythmic that can cause Torsade de Pointes (TdP) and therefore requires frequent monitoring of renal function, electrolytes and electrocardiography. The purpose of this study is to evaluate adherence to an institution-specific sotalol-use protocol and assess the effect of protocol adherence on patient outcomes.

Methods

This retrospective chart review examined all adult patients at Memorial Regional Medical Center (MRMC) that received a dose of sotalol between May 2014 and April 2015. The following data was collected: patient age, gender, height, weight, creatinine clearance, serum electrolyte levels (potassium and magnesium), sotalol dose, indication, interacting medications, QTc/ JTc intervals, pharmacist recommendations and whether the patient was a new start or a continuation of therapy. Data was used to compare the impact of hospital protocol and pharmacy recommendations on patient outcomes. Additionally, trends in electrolytes and corrections were examined.

Results

Of the 120 admissions examined, 64 (53%) were managed according to MRMC protocol (figure 1). TdP did not occur during the study period. Patients managed according to protocol had a mean QTc of 456 ms vs. 483 ms in the protocol non-adherent group (p=0.003). Physicians accepted 42 of 71 (59%) pharmacy recommendations. Mean electrolyte concentrations between groups showed no statistical difference.

Conclusion

Non-adherence to protocol was not associated with an increased incidence of TdP however QTc intervals were significantly longer in the protocol non-adherent group than the protocol adherent group.

Background

Sotalol is a cardiac antiarrhythmic indicated for the treatment of atrial fibrillation, a trial flutter and life threatening ventricular arrhythmias [1]. It has class III (action potential prolonging) and class II (beta blocking) properties. This action potential prolonging effect results from blockade of the rapid component of the delayed rectifier potassium current (IKr). Due to its action potential prolonging effects it can cause Torsades de Pointes (TdP) which is a sometimes fatal cardiac arrhythmia that is usually precipitated by a combination of QTc prolongation and electrolyte deficiency. A review published in 1996 that examined 3135 adult patients on oral d,l-sotalol showed an incidence of 1.9% for TdP [2]. This study also showed that women and patients with elevated serum creatinine were at a greater risk for developing TdP. As a result sotalol requires close monitoring of patients’ renal function, electrolyte levels (magnesium and potassium) and electrocardiograph. The purpose of this study is to evaluate adherence to an institution-specific sotalol-use protocol and assess the effect of protocol adherence on patient outcomes.
Memorial Regional Medical Center (MRMC) is a 225-bed acute care hospital located in Mechanicsville, VA. The MRMC protocol for patients newly initiated on sotalol requires baseline EKG monitoring as well as 2-4 hours after each dose of sotalol. Pharmacy is responsible for entering notes in the medication administration record to remind nursing staff to perform this monitoring. Electrolytes (magnesium and potassium) should be monitored at least daily and corrected as necessary to maintain a serum magnesium level above 2 mEq/L and a serum potassium level above 4 mEq/L. Renal function should be monitored closely given that sotalol is a renally adjusted medication. Patients should not be discharged until they have tolerated 6 doses in the hospital in order to ensure they are stable prior to being sent home. The protocol for patients who are continued on sotalol started prior to admit is less stringent. These patients should receive only periodic EKG monitoring along with renal function and electrolyte monitoring. If the patient’s QTc becomes prolonged the dose should be reduced or held until it returns to normal. Specifically, a QTc of > 520 ms in a trial arrhythmias and > 550ms in ventricular arrhythmias should warrant consideration of dose reduction or discontinuation. The pharmacist’s role throughout this process is to monitor patients, ensure these criteria are met and contact the appropriate prescriber or nurse if they are not.

A prospective study, published by Finks and colleagues, examined 36 patients who received sotalol and assessed patient outcomes with regards to pharmacist involvement. Pharmacists followed these patients and made recommendations for renal adjustment when necessary. The study found that 89% of patients were receiving inappropriate doses of sotalol based on their renal function. Recommendations regarding dose adjustment were accepted 50% of the time. As a result of the study it was recommended that sotalol be added to the pharmacy automatic renal adjustment program.

**Methods**

This study is a single-center, retrospective, chart review of 133 patients between May 2014 and April 2015. This study was approved by the Bon Secours Institutional Review Board. Patients were included if they were over the age of 18 years and received sotalol while admitted to the hospital. Patients were excluded if they did not have a documented QTc in their medical record. The primary endpoint of the study was the percentage of patients managed according to protocol. Secondary endpoints included incidence of TdP, difference in mean QTc between the protocol adherent and protocol non-adherent groups, percentage of pharmacy recommendations accepted by the physician and difference in mean electrolyte concentrations between groups. Data was collected and analyzed using descriptive statistics and two-sample t-tests for continuous data.

**Results**

Of 133 total patient encounters, 120 were included in the final analysis as 13 patients were excluded due to not having a documented QTc. Baseline characteristics between groups were similar however more patients in the protocol non-adherent group were new starts (60.7%) compared with the protocol adherent group (10.9%). The majority of patients were receiving sotalol for the management of a trial arrhythmias: 85.9% of the protocol adherent group and 82.1% of the protocol non-adherent group. Drug interactions that had the potential to worsen patient outcomes were identified in 50% of the protocol adherent group and 50% of the protocol non-adherent group. The most commonly implicated interacting medications were ondansetron and loop diuretics such as furosemide and bumetanide (table 1).

For the primary endpoint, 64 (53%) patients were managed according to protocol whereas 56 (47%) had some deviation. Of the protocol non-adherent group 17 were dosed inappropriately based on renal function or a prolonged QTc, 33 patients required electrolyte repletions, 13 were discharged prior to their 6th dose, 5 patients were contraindicated for the use of sotalol and 3 were excluded due to not having properly measured QTc segments (figure 2). Of the 5 patients who were contraindicated, pharmacy made recommendations on 4 of the patients however all of these recommendations were rejected by the physician and the patients were continued on sotalol. The mean maximum QTc was significantly shorter in the protocol adherent group (456 ms) versus

**Table 1**

<table>
<thead>
<tr>
<th></th>
<th>Protocol Adherent (n=64)</th>
<th>Protocol Non-Adherent (n=56)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male (%)</td>
<td>62.5</td>
<td>57.1</td>
</tr>
<tr>
<td>Age (mean, years)</td>
<td>66.1</td>
<td>67.9</td>
</tr>
<tr>
<td>CrCl (mean, mL/min)</td>
<td>74.8</td>
<td>67.1</td>
</tr>
<tr>
<td>New Start (%)</td>
<td>10.9</td>
<td>60.7</td>
</tr>
<tr>
<td>Type of Arrhythmia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atrial (%)</td>
<td>85.9</td>
<td>82.1</td>
</tr>
<tr>
<td>Ventricular (%)</td>
<td>9.4</td>
<td>10.7</td>
</tr>
<tr>
<td>Both (%)</td>
<td>4.7</td>
<td>7.1</td>
</tr>
<tr>
<td>Mean Daily Dose (mean, mg)</td>
<td>177.4</td>
<td>178.8</td>
</tr>
<tr>
<td>Patients with Drug Interaction(s) (%)</td>
<td>50</td>
<td>50</td>
</tr>
</tbody>
</table>


the protocol non-adherent group (483 ms) (P=0.003) (figure 3). TdP did not occur in either group during the study period. There was no significant difference between the protocol adherent and protocol non-adherent groups with regard to potassium (4.01, 3.98; P=0.76) and magnesium levels (1.85, 1.79; P=0.44) (figure 4).

Of 71 pharmacy recommendations made, 42 were accepted (59% acceptance). Recommendations included electrolyte repletions, dose adjustments, discontinuation of therapy and adjusting for drug interactions (Figure 5).

**Discussion**

No association can be made between adherence to protocol and the likelihood of TdP given that this complication did not occur during the study period. This is not surprising given the rarity of this complication and relatively small sample size of the study. This study does demonstrate an association between non-adherence to protocol and prolonged QTc segments which in combination with electrolyte deficiency, acute renal failure and drug-drug interactions has the potential to precipitate TdP. The majority of new starts were not managed according to protocol which might be explained by the more stringent nature of the protocol for new initiates. Prior to this study being conducted but after the study period, an automatic pharmacy electrolyte repletion protocol was implemented to minimize the number of patients with electrolyte deficiencies. This has made it easier for the pharmacist to replete electrolytes without having to contact the prescriber and request permission.

There were several limitations of this study including that it was a retrospective chart review with a small sample size. Given the quantity of EKG measurements that were required by the protocol (particularly with new starts), it was not feasible to document a new EKG strip for each patient in the electronic medical record, each time the nurse needed to record it. The most efficient method to obtain these measurements was for the nurse to document them manually. The data collected for my study was taken from these nursing notes as opposed to being extracted directly from the EKG strip; given this method, the accuracy of these measurements cannot be validated. Additionally, this has the potential to cause random error as the nurse carries over the information manually into the chart. This would also falsely elevate the number of
patients managed according to protocol since the patients who did not have documented QTc segments were excluded from the data set. Another limitation is that the nursing protocol for measuring QTc is unclear. The nurses are expected to take a measurement from the same lead three or more times, calculate an average of the measurements and report the result. However, there is no way to confirm that the nurses were consistently following this protocol which could contribute to variability in the reported results.

**Conclusion**

Non-adherence to protocol was not associated with an increased risk of TdP; however mean QTc segments were significantly longer in the protocol non-adherent group which in combination with drug interactions, acute renal failure and electrolyte deficiencies puts patients at an increased risk for developing this rare and potentially life-threatening arrhythmia. This study identifies an area for pharmacy to demonstrate an impact on patient safety through continued recommendations regarding dose adjustments.

**References**