INTRODUCTION

Dabigatran, apixaban, and rivaroxaban have become popular alternatives to the standard oral anticoagulant warfarin, which requires frequent monitoring, has significant drug interactions, and has a narrow therapeutic index. Attractive benefits of these agents include the lack of drug level monitoring and less drug interactions. However, there are no target-specific antidotes available and less experience in practice versus warfarin given their inability to measure a specific level of anticoagulation. At DCH Regional Medical Center (RMC) and Northport Medical Center (NMC), these agents are used frequently, but little is known about prescribing patterns and outcomes related to these agents.

PURPOSE

The purpose of this study was to evaluate the appropriateness of dosing for patients receiving oral anticoagulants and the incidence of complications with dosing.

METHODS

Design:
- This study was a medication usage evaluation using patients who received at least one dose of dabigatran, apixaban, or rivaroxaban for treatment of VTE, reduction in risk of VTE, or reduction in risk of stroke following atrial fibrillation at DCH RMC or NMC between January-July 2015.
- Patients were identified using patient–drug utilization reports in Meditech.
- Patients were excluded from the study if they were <19 years of age and received a dose of dabigatran, apixaban, or rivaroxaban for post-op prophylaxis of VTE for hip or knee replacement, for an unknown indication, or an off-label indication not otherwise specified.
- Physician notes were reviewed to determine indication for therapy.
- Evaluation of appropriateness of indication and dosing were determined when a dose was first ordered or adjusted in accordance with recommendations in the product-specific package insert.
- Any documented pharmacy interventions regarding anticoagulation were recorded (dose changes, duplications, etc).

Data Collection:
- Collected data included age, gender, weight, SCR, indication, dose, frequency, use of anticoagulant as home medication, use of other anticoagulants, interacting drugs, bleeding events (defined as ≥2g/dL decrease in hemoglobin, transfusions ≥2 packed red blood cells, confirmed bleeding source resulting in fatal outcome, confirmed bleed in critical anatomic site or retroperitoneal site), or thrombotic events (defined as confirmed VTE or embolic stroke by imaging studies or documentation in chart).
- Patients were followed for 30 days from date of discharge to assess for readmission from any cause. Any complications (bleeding or thrombotic events) were noted.

RESULTS

Baseline Characteristics

<table>
<thead>
<tr>
<th>Baseline Characteristics</th>
<th>Dabigatran (n=34)</th>
<th>Apixaban (n=60)</th>
<th>Rivaroxaban (n=60)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, range (years)</td>
<td>73 (55-94)</td>
<td>67 (19-96)</td>
<td>67 (31-92)</td>
</tr>
<tr>
<td>Gender (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>52</td>
<td>35</td>
<td>53</td>
</tr>
<tr>
<td>Female</td>
<td>48</td>
<td>65</td>
<td>47</td>
</tr>
<tr>
<td>Laboratory Data (mean)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TBW (kg)</td>
<td>91.47</td>
<td>90.75</td>
<td>92.24</td>
</tr>
<tr>
<td>SCR (mg/dL)</td>
<td>1.16</td>
<td>1</td>
<td>1.06</td>
</tr>
<tr>
<td>CrCl (mL/min)</td>
<td>59</td>
<td>64</td>
<td>61</td>
</tr>
<tr>
<td>Home Medications (%)</td>
<td>Yes</td>
<td>88</td>
<td>45</td>
</tr>
</tbody>
</table>

Appropriateness of Dosing of Novel Oral Anticoagulants

<table>
<thead>
<tr>
<th>Treatment DVT/PE</th>
<th>Dabigatran (23/34 (70))</th>
<th>Apixaban (10/60 (50))</th>
<th>Rivaroxaban (60/60 (77))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduction risk DVT/PE</td>
<td>3/5 (60)</td>
<td>3/5 (60)</td>
<td>13/15 (87)</td>
</tr>
<tr>
<td>Stroke Prophylaxis Afib</td>
<td>2/6 (33)</td>
<td>2/6 (33)</td>
<td>9/9 (89)</td>
</tr>
</tbody>
</table>

Complications

- Embolic stroke
  - Dabigatran 0
  - Apixaban 0
  - Rivaroxaban 0
- Hb decrease ≥2g/dL
  - Dabigatran 1
  - Apixaban 2
  - Rivaroxaban 3

Clinical Interventions

- Accepted
  - Dabigatran 0
  - Apixaban 0
  - Rivaroxaban 0
- Not Accepted
  - Dabigatran 1
  - Apixaban 1
  - Rivaroxaban 0

Readmissions

- Dabigatran 6
- Apixaban 10
- Rivaroxaban 1

DISCUSSION

- Novel oral anticoagulants used most often for stroke prophylaxis in atrial fibrillation
- Only 50% of prescribing appropriate for apixaban, including only 33% of appropriate prescribing for reduction in risk of DVT/PE
- Majority of errors in dosing related to renal function
- Potential confusion over criteria used for dosage adjustment with atrial fibrillation patients
- Frequent use of concomitant antiplatelet agents
- Seven total treatment doses of parenteral anticoagulants before switching to oral anticoagulation, 2 possible bridging scenarios
- Five pharmacy clinical interventions, 4 accepted
- Low rate of complications in all groups
- Of the complications, only two patients were receiving inappropriate dosing
- Only 2/23 readmissions potentially due to anticoagulant complications

FUTURE STEPS

- This study allowed the researchers to examine prescribing patterns at DCH RMC and NMC in regards to select oral anticoagulants and identify areas where prescribing can be improved to ensure appropriate use
- Shed light into improving renal dosing programs for pharmacists to aid with selection of appropriate dosing
- Future steps to evaluate appropriateness of dosing upon discharge and evaluate the appropriateness of dosing while outpatient using transitions of care model

CONCLUSIONS

- Inappropriate prescribing more likely with apixaban dosing and adjustments for renal function for all anticoagulants
- Low risk of complications regardless of dose appropriateness, but could be due to lower sample size and inpatient monitoring only
- Opportunity for education regarding dose adjustments for oral anticoagulants

References available upon request