Comparative Bleeding Rates & Associated Factors In Patients Receiving Oral Anticoagulant Therapy

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Disclosure

• Nothing to disclose
Objectives

• Compare and contrast the Novel Oral Anticoagulant (NOAC) agents and warfarin
• Identify tools used to define and assess risk of bleed for patients receiving oral anticoagulation
• Discuss bleeding rates among oral anticoagulation agents based on the results of the investigation discussed
Mobile Infirmary Medical Center (MIMC)

- Located in Mobile, Al
- 669 Beds
- Primarily Adults
- Acute care
Background

• Anticoagulation is necessary in several conditions

• Identifying bleeding rates and risk factors can balance safety & efficacy

• Oral anticoagulants (OAC) offer:
  – Convenience over parenteral anticoagulation
  – Newer OACs ➔ multiple targets of action
Background

• Newer OACs compared to warfarin:
  – More predictable PK
  – Shorter half lives
  – Fewer food and drug interactions
  – Lower rates of intercranial hemorrhage (ICH) and fatal bleed

• However...
  – Renal impairment of greater concern
  – Bleed rates variable
  – Limited reversal options
Background

• Tools for **defining** bleed: • **Assessing risk** of bleed:
  – TIMI
  – GUSTO
  – ISTH
  – HAS-BLED
  – ATRIA
  – ORBIT

• Major trials identified independent risk factors for bleed:
  – ARISTOTLE
  – ROCKET-AF
  – RE-LY
Purpose

• Capture bleeding rates among inpatients receiving oral anticoagulation (OAC) at Mobile Infirmary Medical Center (MIMC)

• Determine how well risk factors are being identified, allowing for earlier screening and intervention
Objectives

• **Primary Objective**: Compare rates of bleed among patients receiving OAC in the inpatient setting

• **Secondary Objective**: Identify potential risk factors associated with bleeding in real-world patient populations
Design

• Retrospective cohort study

• Reviewed inpatients at MIMC who received oral anticoagulants

• Study period: January 1 to June 30, 2017
Methodology

Inclusion/Exclusion Criteria

Inclusion Criteria
- Received warfarin, apixaban, dabigatran, rivaroxaban, or edoxaban while hospitalized at MIMC
- Experienced a bleed while on an OAC during hospitalization
- ≥18y/o

Exclusion Criteria
- Abnormal coagulation without a bleed
- Received OAC without subsequent bleed
- Present to the ED with a bleed after being discharged home from MIMC on an OAC ≥72hrs previously
Methodology

• A retrospective chart review was conducted on those who met inclusion to evaluate the severity of bleed experienced and identify risk factors

• Collection criteria based upon:
  – Validated risk assessment tools for bleed:
    • HAS-BLED, ATRIA, & ORBIT
  – Validated definitions of bleed:
    • TIMI, GUSTO, & ISTH
  – Independent risk factors identified in major trials:
    • Age, PMH, CrCl, ASA, NSAID, Sex, Weight, Elevated DBP
553 pts. Received OAC during the time frame

Evaluated for signs and symptoms or treatment of bleed

54 pts. (9.8%) met inclusion

Chart review to investigate nature of bleed

Evaluation: Bleeding rates Risk factors for bleed

- ICD 10 codes for signs and symptoms of bleed
- Medication charge codes for treatments of bleed
- Charge codes for blood products received

- Fell into one of the three definitions of bleed
- Bleed risk assessment tools
- Major trials
- Drug interactions
Results

Baseline Characteristics

Average Age: 72.8 (48-95) years
Sex: 24 Male (44%)

Race, n (%)
- Black 22 (41)
- White 31 (57)
- Hisp. 1 (1.9)

Reason for Anticoagulation, n (%)
- Atrial Fibrillation (AFib) 27 (50)
- Deep Vein Thrombosis (DVT) 13 (24)
- Pulmonary Embolism (PE) 2 (3.7)
- Surgical Prophylaxis 2 (3.7)
- Mitral Valve Replacement (MVR) 4 (7.4)
- Unclear 6 (11)
## Results
### Primary Endpoint

<table>
<thead>
<tr>
<th>Medication</th>
<th>% Among 54pts. that Suffered Bleed; n, (%)</th>
<th>% Among Individual OACs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td># on Agent</td>
</tr>
<tr>
<td>Warfarin</td>
<td>26 (48)</td>
<td>217</td>
</tr>
<tr>
<td>Apixaban</td>
<td>20 (37)</td>
<td>179</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>7 (13)</td>
<td>146</td>
</tr>
<tr>
<td>Dabigatran</td>
<td>1 (2)</td>
<td>14</td>
</tr>
<tr>
<td>Edoxaban</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

### Top Three Bleeding Events, n(%)

<table>
<thead>
<tr>
<th>Event</th>
<th>Count, (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive Fecal Occult</td>
<td>23, (43)</td>
</tr>
<tr>
<td>Hematuria</td>
<td>4, (7)</td>
</tr>
<tr>
<td>Rectal Bleed</td>
<td>4, (7)</td>
</tr>
</tbody>
</table>
## Results

### Secondary Endpoints

<table>
<thead>
<tr>
<th>TIMI</th>
<th>GUSTO</th>
<th>ISTH</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MINOR</strong></td>
<td>11 (20)</td>
<td>24 (44) <strong>MILD</strong></td>
</tr>
<tr>
<td><strong>MINIMAL</strong></td>
<td>39 (72)</td>
<td><strong>MODERATE</strong> 27 (50)</td>
</tr>
<tr>
<td><strong>MAJOR</strong></td>
<td>2 (4)</td>
<td><strong>SEVERE</strong> 1 (2)</td>
</tr>
<tr>
<td><strong>NA</strong></td>
<td>1 (2)</td>
<td><strong>NA</strong> 2 (4)</td>
</tr>
</tbody>
</table>

**RELEVANT BUT MINOR** 37 (69)

**FATAL/POTENTIALLY FATAL** 12 (22)

**NA** 5 (9)
## Results

### Secondary Endpoints

<table>
<thead>
<tr>
<th>PMH, n (%)</th>
<th>COPD</th>
<th>HTN</th>
<th>PAD</th>
<th>MI</th>
<th>Stroke</th>
<th>TIA</th>
<th>GIB</th>
<th>Bleed</th>
<th>Obesity</th>
</tr>
</thead>
<tbody>
<tr>
<td>COPD</td>
<td>18 (33)</td>
<td>20 (37)</td>
<td>11 (20)</td>
<td>7 (13)</td>
<td>4 (7)</td>
<td>6 (11)</td>
<td>5 (9)</td>
<td>3 (5)</td>
<td>17 (31)</td>
</tr>
</tbody>
</table>

**Concomitant Aspirin Use Among Bleeds (Total of 20 pts.)**

<table>
<thead>
<tr>
<th>Type of Bleed</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>GI Bleed</em>, n (%)</td>
<td>15 (75)</td>
</tr>
<tr>
<td><em>Non-GI bleed</em>, n (%)</td>
<td>5 (25)</td>
</tr>
<tr>
<td><em>GI prophylaxis among GI bleed</em>, n (%)</td>
<td>17 (85)</td>
</tr>
<tr>
<td><em>No GI prophylaxis</em>, n (%)</td>
<td>3 (15)</td>
</tr>
</tbody>
</table>
Discussion

• The sample size did not allow for statistical comparisons between agents

• Expanding the study period would allow for a better overall comparison between OAC agents.
Summary

• Overall, a low rate of bleeding events occurred among patients receiving OAC

• Most bleeds fell outside the criteria for major bleed

• Although sample size was too small to draw conclusions, it was observed that bleeding events were equivalent between warfarin and apixaban
Acknowledgements

• I would like to take the time to acknowledge those who helped and supported the completion of this project

– Research Advisors
  • Michael J. Scalese, Pharm.D., BCPS, CACP
  • Charles E. DuRant Jr., Pharm.D.
  • Oscar J. Umbehagen, Pharm.D.
Self-Assessment Question

• Based on the results of this investigation, which of the following statements concerning bleeding rates of OAC in a community hospital setting is true?

a) Warfarin had the highest percentage of bleeds observed
b) Warfarin and apixaban had the highest percentage of bleeds observed
c) Dabigatran had the lowest percentage of bleeds observed
d) Both B & C

Rivaroxaban had the lowest observed rate of bleed
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