The risk of gastrointestinal bleeding with novel oral anticoagulants in a large cohort of patients at a district general hospital

Aditi Kumar1, Benjamin R Disney1, Rupert Hipkins2, Sarah Hughes2, Steven Jenkins2, & Sauid Ishaq1

1Department of Gastroenterology, Dudley Group NHS Foundation Trust, Russells Hall Hospital, Dudley UK
2Department of Haematology, Dudley Group NHS Foundation Trust, Russells Hall Hospital, Dudley UK

BACKGROUND:

- Rivaroxaban, apixaban and dabigatran compile the novel oral anticoagulants (NOAC).
- NOACs are used as first line treatment for atrial fibrillation (AF), pulmonary embolism (PE) at Russells Hall Hospital (RHH) since 2012 and deep venous thrombosis (DVT) since 2013
- Trial data regarding risk of gastrointestinal (GI) bleeding is conflicting
  - In the ROCKET-AF study the rate of GI bleeding was significantly higher in the group randomised to receive rivaroxaban (3.2%) versus warfarin (2.2%, p = 0.001)
  - EINSTEIN-DVT and EINSTEIN-PE studies showed similar bleeding rates for rivaroxaban and warfarin although GI bleeding was not specifically addressed
- A meta-analysis of NOACs found an increased risk of GI bleeding with NOAC as opposed to warfarin (2.3% vs 1.3%, p = 0.036)
- Although trials have shown increased risk of GI bleeding with NOACs, little is known about its incidence in the real world setting
- We aimed to ascertain the incidence of GI bleeding, endoscopic findings, time of onset of bleeding and need for intervention in patients commencing NOACs

METHODS:

- A retrospective review was performed of all patients at RHH who received NOACs
- These patients were identified from the anticoagulation database and cross referenced with the GI endoscopy database and patient notes.
- Basic demographic, clinical and laboratory data and endoscopic findings were collated.

STRENGTHS:

- Largest cohort worldwide
- Single center experience

LIMITATIONS:

- Due to the small sample size of patients on apixaban and dabigatran, difficult to compare with the trial data as well as between the NOACs
- Seventy of upper GI bleed using the Rockall score or Blatchford score was not performed
- A multivariate analysis needs to be performed with patients on warfarin over the same time period at RHH to ensure there are no confounding variables
- Alcohol, concomitant medications, symptoms, comorbidities

CONCLUSIONS:

- Prevalence of bleed more common >75 yrs of age
- Whilst there appeared to be a higher incidence of GI bleeding as compared to that observed in RCTs thus far:
  - There were no deaths directly as a result of the GI bleed
  - Only 11.5% required endoscopic intervention
  - The use of blood products was relatively low at 34.4%
  - Further studies need to be performed to provide a more accurate analysis for apixaban and dabigatran

REFERENCES:


RESULTS

Table 1: Comparison between the NOACs

<table>
<thead>
<tr>
<th>NOACs</th>
<th>Non-bleeders (n= 144)</th>
<th>Bleeders (n= 61)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (yr)</td>
<td>74 +/- 15</td>
<td>80 +/- 8</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Females 137 (95.3%)</td>
<td>60 (100%)</td>
<td></td>
</tr>
<tr>
<td>Males 14 (9.9%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>NOAC therapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rivaroxaban 2332</td>
<td>Rivaroxaban 54 (88.5%)</td>
<td></td>
</tr>
<tr>
<td>Apixaban 77 (5.3%)</td>
<td>Apixaban 4 (6.6%)</td>
<td></td>
</tr>
<tr>
<td>Dabigatran 77 (5.1%)</td>
<td>Dabigatran 3 (4.9%)</td>
<td></td>
</tr>
</tbody>
</table>

Table 2: Bloods on admission

<table>
<thead>
<tr>
<th>INR &gt; 2</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>INR &gt; 1.5</td>
<td>26.2%</td>
</tr>
<tr>
<td>INR &gt; 2</td>
<td>14.7%</td>
</tr>
<tr>
<td>Hb &lt; 10</td>
<td>49.2%</td>
</tr>
<tr>
<td>Hb &lt; 7</td>
<td>16.7%</td>
</tr>
</tbody>
</table>

*2.45% bleeds in total at time of study. Since then, increased to 2.57%

Table 3: Endoscopy findings upper GI vs lower GI bleeds

<table>
<thead>
<tr>
<th>Upper GI bleed* (n)</th>
<th>Lower GI bleeds** (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal (6)</td>
<td>Diverticular disease (16)</td>
</tr>
<tr>
<td>Peptic ulcer disease (6)</td>
<td>Haemorrhoids (12)</td>
</tr>
<tr>
<td>Gastritis (6)</td>
<td>Polyps (colonic/rectal) (7)</td>
</tr>
<tr>
<td>Oesophagitis (5)</td>
<td>Normal (5)</td>
</tr>
<tr>
<td>30/61 (49.2%)</td>
<td>*31/61 (51.8%)</td>
</tr>
<tr>
<td>16/30 (53%)</td>
<td>5/11 (45%)</td>
</tr>
<tr>
<td>*Fisher’s test</td>
<td></td>
</tr>
</tbody>
</table>

ALL PATIENTS ON NOACs:

- The most common type of bleed presentation was PR bleeding (48%) followed by melaena (37%), haematemesis (10%) and coffee ground vomiting (6%)

Conclusions:

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REFERENCES:


MORTALITY

30 day mortality rate was 10.9% (n=11)

No deaths due to severe GI haemorrhage

Causes of death:
- Cancer
- Septis
- Unknown
- Pneumonia

Graph 1: Endoscopic findings of all patients on NOACs

- 26.2% patients with endoscopic findings compatible with active/recent bleeding
- 11.5% patients had active bleeding at time of endoscopy, all treated successfully

Graph 2: Risk of bleeding between NOACs

- Risk of bleeding
- Clinical significance

<table>
<thead>
<tr>
<th>NOAC</th>
<th>Non Bleeders</th>
<th>Bleeders</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dabigatran vs Apixaban</td>
<td>NS (p = 0.71)</td>
<td></td>
</tr>
<tr>
<td>Apixaban vs Rivaroxaban</td>
<td>NS (p = 0.43)</td>
<td></td>
</tr>
<tr>
<td>Dabigatran vs Rivaroxaban</td>
<td>5% vs 2%, p = 0.11</td>
<td></td>
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</tbody>
</table>

Graph 3: Age range of all patients that had a bleeding episode whilst on NOAC. Median age was 79.6