Anticoagulants: New and Old

Dr. David Carr
February 23rd 2014
Objectives: Anticoagulants

- Nailing down the challenges docs face in dealing with patients on warfarin
- Introducing the newish agents
- Reversing the beasts
Case 1: The referral

- 50 y.o male sent in to the ER because of an INR of 6
  - Asymptomatic
  - Hx AFIB
  - Recent GI illness

- What are the recommendations for reversing?
## Warfarin Reversal

<table>
<thead>
<tr>
<th>INR</th>
<th>HOLD</th>
<th>PO VIT K</th>
<th>IV VIT K</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.5-10</td>
<td>YES</td>
<td>NO ADVANTAGE TO USE VIT K (IIB)</td>
<td>NO ADVANTAGE TO USE VIT K</td>
</tr>
<tr>
<td>&gt; 10</td>
<td>YES</td>
<td>1-2.5mg (IIC)</td>
<td>NO</td>
</tr>
<tr>
<td>BLEEDING</td>
<td>YES</td>
<td>NO</td>
<td>5-10MG IV SLOW</td>
</tr>
</tbody>
</table>

Holbrook A et al. *Chest.* 2012; 141(2 suppl):e152s-84s
## Monitoring the abnormal INR

<table>
<thead>
<tr>
<th>INR Result</th>
<th>Action to maintain target INR</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1.5</td>
<td>Increase weekly dose by 10-20%</td>
</tr>
<tr>
<td>1.5-1.9</td>
<td>Increase weekly dose by 5-10%</td>
</tr>
<tr>
<td>2-3</td>
<td>NO change</td>
</tr>
<tr>
<td>3.1-3.5</td>
<td>Decrease weekly dose by 5-10%</td>
</tr>
<tr>
<td>3.6-4.9</td>
<td>Hold one dose, decrease weekly dose by 10-20%</td>
</tr>
<tr>
<td>5-9</td>
<td>Hold 2 doses, decrease weekly dose by 10-20%</td>
</tr>
<tr>
<td>&gt;9</td>
<td>Urgent evaluation, consider vitamin K po</td>
</tr>
</tbody>
</table>

*University of Wisconsin-Madison Health 2013*
Case 2: The liver patient

- 66 y.o hep C cirrhotic patient comes in with ascites and melena
- INR 1.8 → not on any anticoagulants
Case 2: The liver patient

- INR’s are often elevated
- Patients are still able to clot → dec protein c/s
- If life threatening bleed and Increased INR → consider FFP
- Routine use of FFP or PCC not recommended
- No role for PCC for mixed coagulopathy
Case 3: Minor head injury

66 y.o male
Slipped on ice
Small hematoma
INR 2.7
CT negative

What to do?
Case 3: Minor head injury

- Prospective trial: 97 minor HI’s on warfarin
- 16% positive CT’s initially
- Negs: Observation unit for 24hrs w/ repeat CT
  - Delayed bleed in 6% (5 pts) on repeat CT at 24hr
    - 2 of them d/c, 3 admitted→ 1 craniotomy
  - Of the pts who went home after 2 negative CT at 24hr
    - 1 SDH at 2 days and 1 SDH at 8 days

Case 3: Minor head injury

- Delayed bleed approximately 6%
- Can occur > week later
- **Elderly and INR >3 → OR 14!** for risk re-bleed
- There are no clear evidenced based answers
  - Adjusting anticoagulation?
  - Repeat CT head?
  - Observe?
- Explain to patients risk of re-bleed
The Hidden Assassin: Plavix

- Prospective observational study 1064 pts
- Minor head injuries on warfarin or plavix
- 90% got CT → 12% bleed plavix & 5% warfarin
- Delayed bleed 0% plavix and 0.6% warfarin

RESPECT PLAVIX

Nishijima et al  Ann Emerg Med 2012 June 59 (6) 460-8
## Case 4: Severe HI & INR 3

<table>
<thead>
<tr>
<th>Properties</th>
<th>PCC</th>
<th>FFP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset</td>
<td>Rapid within 15 minutes</td>
<td>Slow</td>
</tr>
<tr>
<td></td>
<td>Wears off in 4-8 hours</td>
<td>Large volumes</td>
</tr>
<tr>
<td>Dose</td>
<td>INR 1.5-3 → 1000 units</td>
<td>Inactive FFP</td>
</tr>
<tr>
<td></td>
<td>INR 3-5 → 2000 units</td>
<td></td>
</tr>
<tr>
<td></td>
<td>INR &gt; 5 → 3000 units</td>
<td></td>
</tr>
<tr>
<td></td>
<td>INR Unknown → 2000 units</td>
<td></td>
</tr>
<tr>
<td>Vitamin K</td>
<td>10 mg IV over 30 minutes</td>
<td>10 mg IV over 30 minutes</td>
</tr>
</tbody>
</table>

**PCC FOR ALL LIFE THREATENING BLEEDS**
THE DECISION TO USE PCC VS FFP IS NOT FINANCIAL
New kids on the block

• Pros
  – No monitoring
  – Minimal drug interactions
  – Rapid onset → no bridging

• Cons
  – Difficulty assessing treatment effect and compliance
  – Renal dose adjustments
  – Reversibility
  – GI problems
## Reversing the Beasts

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<thead>
<tr>
<th>CHARACTERISTICS</th>
<th>WARFARIN</th>
</tr>
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<tbody>
<tr>
<td>MECHANISM OF ACTION</td>
<td>VIT K ANTAGONIST</td>
</tr>
<tr>
<td>T1/2</td>
<td>20-60hrs</td>
</tr>
<tr>
<td></td>
<td>Duration 2-5 days</td>
</tr>
<tr>
<td></td>
<td>Therapeutic 50-60%</td>
</tr>
<tr>
<td>DRUG INTERACTION</td>
<td>MANY</td>
</tr>
<tr>
<td>MONITORING</td>
<td>INR/PT</td>
</tr>
<tr>
<td>REVERSING AGENT</td>
<td>ALWAYS VIT K REVERSED IN 24HR</td>
</tr>
<tr>
<td></td>
<td>FFP-SLOW</td>
</tr>
<tr>
<td></td>
<td>PCC/APCC- RAPID</td>
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The Comparisons

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<th>DABIGATRIN</th>
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<tr>
<td>MECHANISM OF ACTION</td>
<td>VIT K ANTAGONIST</td>
<td>DIRECT THROMBIN INHIBITOR</td>
</tr>
<tr>
<td>T1/2</td>
<td>20-60hrs Duration 2-5 days</td>
<td>14-16 hr (CrCl&gt;80) Peak 1hr</td>
</tr>
<tr>
<td>DRUG INTERACTION</td>
<td>MANY</td>
<td>FEW</td>
</tr>
<tr>
<td>MONITORING</td>
<td>INR/PT</td>
<td>THROMBIN TIME</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PTT</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cr</td>
</tr>
<tr>
<td>REVERSING AGENT</td>
<td>ALWAYS VIT K REVERSED IN 24HR</td>
<td>AC DIALYZABLE</td>
</tr>
<tr>
<td></td>
<td>FFP-SLOW, VOLUME PCC/APCC- RAPID</td>
<td>APCC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cyclokapron</td>
</tr>
<tr>
<td></td>
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<td>rFVIIa</td>
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<th>RIVAROXABAN. APIXABAN</th>
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<td>VIT K ANTAGONIST</td>
<td>DIRECT THROMBIN INHIBITOR</td>
<td>ANTI Xa INHIBITOR</td>
</tr>
<tr>
<td>T1/2</td>
<td>20-60hrs Duration 2-5 days</td>
<td>14-16 hr (CrCl&gt;80) Peak 1hr</td>
<td>Riv- 5-9hr Apix- 8-15hr</td>
</tr>
<tr>
<td>DRUG INTERACTION</td>
<td>MANY</td>
<td>FEW</td>
<td>FEW</td>
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<td>MONITORING</td>
<td>INR/PT</td>
<td>THROMBIN TIME PTT Cr</td>
<td>ANTI Xa INR, PT Cr</td>
</tr>
<tr>
<td>REVERSING AGENT</td>
<td>ALWAYS VIT K REVERSED IN 24HR FFP-SLOW, VOLUME PCC/APCC- RAPID</td>
<td>AC DIALYZABLE APCC Cyclokapron rFVIIa</td>
<td>NON DIALYZABLE PCC/APCC Cyclokapron rFVIIa</td>
</tr>
</tbody>
</table>
Reversing the new guys
Patient with bleeding on dabigatran

- When was last dose?
- CBC, creatinine
- aPTT*

If aPTT ≥ 40 sec, consult TE or Transfusion Medicine

Mild bleeding
- Local hemostatic measures
- Hold 1 or more doses of dabigatran

Moderate-severe bleeding
- Manage bleeding (compression, surgery)
- Fluid → diuresis
- Transfuse RBCs or platelets if needed (follow Sunnybrook guidelines)
- Oral charcoal if overdose <2 hrs before

Life-threatening bleeding
- Contact Transfusion Medicine
- Tranexamic acid (1 g iv followed by 1 g infusion over 8 hours)
- Urgent hemodialysis might be helpful
- Consider PCC

1. DO NOT TRANSFUSE plasma to reverse ↑ aPTT.
2. Life-threatening bleeding – consider activated PCCs (FEIBA) or PCCs (Octaplex or Beriplex)
   Dose – 50 IU/kg for both products

Patient with bleeding on rivaroxaban

- When was last dose?
- CBC, creatinine
- PT* (not INR)

If PT ≥ 15 sec, consult TE or Transfusion Medicine

Mild bleeding
- Local hemostatic measures
- Hold 1 dose of rivaroxaban

Moderate-severe bleeding¹
- Manage bleeding (compression, surgery)
- Fluid → diuresis
- Transfuse RBCs or platelets if needed (follow Sunnybrook guidelines)
- Oral charcoal if overdose <2 hrs before

Life-threatening bleeding¹
- Contact Transfusion Medicine
- Tranexamic acid (1G IV followed by 1G infusion over 8 hours)
- Consider PCC²

¹DO NOT TRANSFUSE plasma or cryo to reverse ↑ PT
²PCC (Octaplex / Beriplex) 50 IU/kg (each vial = 500 IU)


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Case 4: The Bonus Case

• 30 y.o female presents to the ER after stating she ingested 28 g of rat poison – 6 pucks
• Yes, grams
• What do you want to do

a) Put down the chart as you saw her last week
b) Charcoal and a lot of vitamin K
c) PCC and vitamin K
d) See what the regional poison centre thinks
Case 4: The Bonus Case

• “It will take 24 hours to have an effect, you will be masking it with vitamin K and not really know what’s going on and will have to deal with rebounding INR’s” Dr. Thurgur

• Referred to medicine for serial INR’s and watchful waiting

• INR never changed
Conclusions

• Know how to advise pts with abnormal INR’s
• INR <9→ may not need vitamin K
• Respect plavix
• Advise patients with closed head injuries
• Stay up to date on your hospitals reversal strategies
• Most importantly…….