ALL BLEEDING STOPS...EVENTUALLY!

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NO DISCLOSURES!
OBJECTIVES

• Discuss different types of DOACs
• Discuss the pharmacokinetics of the DOACs
• Discuss strategies for managing bleeding with DOACs
CASE #1

• 67 yo male with PMHx CHF and atrial fibrillation tripped at home and hit his head on the end table.

• Medications – Metoprolol, Lipitor, dabigatran
  • VS HR 140 RR 24 BP 195/115
  • PE: confused, nonfocal, bruising noted over right temporal area, PERRL
    • Irregularly irregular, CTA, No other signs of injury

• Priorities?
  • Airway
  • C-Collar
  • BP management

• Tests/imaging?
CASE #2

• 44 yo male PMHx DM, Obesity, HTN, DVT
• Riding a motorcycle and crashed leading to a deformed, swollen left thigh
• Medications: Norvasc, Pravachol, Coumadin
• VSS HR 130  RR 22 BP 105/45
• Alert, moderate distress, following commands, PERRL, tachycardic, tachypneic, NTND, painful, tight left thigh with temperature difference between right and left foot. Pulses present bilaterally with decreased sensation in the left LE.
• Priorities?
• Labs/imaging
• Treatment options?
CASE #3

- 25 yo female with PMHx of depression and DVT presents after taking a handful of her “blood thinners”.
  - Medications: Xarelto, Zoloft
  - Alert, tearful, nonfocal, RRR, CTA, NTND
  - Priorities?
  - Labs/Tests?
  - Treatment options?
CASE #4

• 71 yo female with PMHx of CHF, CABG, EF 30%, CKD presents with abdominal cramping and lower GI bleed

• Medications: Dabigatran, Zoloft, carvedilol, amiodarone, atorvastatin

• VS HR 60 RR 22 BP 105/50

• Alert, nonfocal, RRR, CTA, NTND, no bruising noted

• Priorities?

• Labs/Tests?

• Treatment options?
CASE #5

- 63 yo male with PMHx of HTN, CKD and Afib presents with chest and back pain.
- Medications: Apixaban, carvedilol,
- VS HR 65 RR 28 BP 115/40
- Alert, nonfocal, IRIRR with holosystolic murmur, CTA, NTND, no bruising noted
- Priorities?
- Labs/Tests?
- Treatment options?
VITAMIN K ANTAGONIST

The diagram illustrates the mechanism of action of vitamin K antagonists, such as warfarin, rivaroxaban, and apixaban, on the coagulation cascade. These agents inhibit various factors and cofactors, as indicated by the crosses in the pathway:

- **Vitamin K antagonists** (e.g., warfarin) inhibit factor Xa, which blocks the conversion of prothrombin to thrombin.
- **Rivaroxaban** and **apixaban** specifically inhibit factor Xa and factor Xa, respectively, without affecting other components of the cascade.
- **Dabigatran** inhibits thrombin directly, preventing the production of fibrin.

The diagram shows the interaction points where these inhibitors act to prevent thrombin formation and fibrin deposition, thus reducing the risk of clot formation.

**Key Components**:
- **XII → XIIa**
- **XI → IX**
- **IXa**
- **IX**
- **VIIa**
- **Xa**
- **X**
- **VIIIa**
- **Prothrombin**
- **Thrombin**
- **Fibrin**
- **Fibrinogen**

The inhibitors block these steps, depicted by the crosses, ensuring that the cascade is halted at critical points.
DOAC – CLASSES

• Direct Thrombin Inhibitor (factor IIa)
  • Dabigatran (Pradaxa)

• Factor Xa inhibitor
  • Rivaroxaban (Xarelto)
  • Edoxaban (Savaysa)
  • Apixaban (Eliquis)
DIRECT THROMBIN INHIBITORS
DIRECT THROMBIN INHIBITORS

- Dabigatran is approved for
  - Nonvalvular afib
  - DVT/PE prophylaxis and treatment
  - Prophylaxis s/p hip and knee surgery

- Pharmicokinetics
  - 12-17 hr ½ life
  - Excretion is 85-90% renal

- Normal TT – NO Dabigatran present
DIRECT THROMBIN INHIBITORS

5 trials with > 27k pts – Afib

• Lower 30 day mortality – 9 vs 13
• Shorter ICU stay – 1.6 vs 2.6

• HIGHER risk of GI bleeding if > 65 –
  • N Engl J Med 2013;368:1272
  • Unmasking of colonic polyps?

• Lower risk of
  • Major bleeding
  • Fatal bleeding
  • Intracranial bleeding
FACTOR XA INHIBITOR

• Rivaroxaban (Xarelto) – Afib/DVT
  • 5-9 hr ½ life
  • Excretion is 35% renal

• Edoxaban (Savaysa) – Afib/DVT
  • 6-11 hr ½ life
  • Excretion is 35% renal

• Apixaban (Eliquis) – Afib/DVT
  • 8-15 hr ½ life
  • Excretion is 25% renal

• SEVERE HEPATIC IMPAIRMENT CAN CAUSE BIO-ACCUMULATION
FACTOR XA INHIBITOR

• Abnormal PT/PTT suggest drug is present
• However, if PT/PTT normal and patient is bleeding
  ASSUME drug is present
• Normal anti-Xa activity strongly excludes drug present
• Apixaban/Eliquis is the ONLY FDA approved DOAC for ESRD
# TREATMENT OPTIONS

## COUMADIN
- Vitamin K
- PCC – 4 and 3 factor
- FFP/Cryoprecipitate
- F7

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## DOACs
- Binding with charcoal
- PCC – 4 factor
- αPCC - FEIBA
- Hemodialysis (dabigatran ONLY)
- Idarucizumab/Praxbind (dabigatran ONLY)
- Anti-fibrinolytic (amicar/tranexamic acid)

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Neurocritical Care Society/Society of Critical Care Medicine Antithrombotic Reversal in Intracranial Hemorrhage Guideline Writing Committee

- October 2012.
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    • Irregularly irregular, CTA, No other signs of injury

• TREATMENTS
  • Aggressive BP control
  • Praxbind
  • PCC – 4 factor (Kcentra)
  • Anti-fibrinolytic
CASE #2

• 44 yo male PMHx DM, Obesity, HTN, DVT

• Riding a motorcycle and crashed leading to a deformed, swollen left thigh

• Medications: Norvasc, Pravachol, Coumadin

• VSS HR 130  RR 22 BP 105/45

• Alert, moderate distress, nonfocal, PERRL, tachycardic, tachypneic, painful, tight left thigh with temperature difference between right and left foot. Pulses present, decreased sensation in the left LE.

• TREATMENTS
  • Vit K and PCC – 4 factor
  • F7 and anti-fibrinolytic (DIC)
CASE #3

• 25 yo female with PMHx of depression and DVT presents after taking a handful of her “blood thinners”.

• Medications: Xarelto, Zoloft

• Alert, tearful, nonfocal, RRR, CTA, NTND

• TREATMENT
  • Charcoal
  • PCC – 4 factor
CASE #4

• 71 yo female with PMHx of CHF, CABG, EF 30%, CKD presents with abdominal cramping and lower GI bleed

• Medications: Dabigatran, Zoloft, carvedilol, amiodarone, atorvastatin

• VS HR 60 RR 22 BP 105/50

• Alert, nonfocal, RRR, CTA, NTND, no bruising noted

• TREATMENTS
  • Charcoal
  • Praxbind
  • PCC – 4 factor
  • HD/CRRT
CASE #5

• 63 yo male with PMHx of HTN, CKD and Afib presents with chest and back pain. Medications: Apixaban, carvedilol,

• VS HR 65 RR 28 BP 115/40

• Alert, nonfocal, IRIRR with holosystolic murmur, CTA, NTND, no bruising noted

• TREATMENTS
  • Charcoal
  • PCC 4 factor or aPCC
  • Anti-fibrinolytic
Not to be outdone by a little solar eclipse, Texas said "Hold my beer & watch this shit!!"
QUESTION #1

• All of the following are recommended in the management of DOAC use and life threatening bleeding:
  • A) FFP
  • B) PCC
  • C) Factor 7
  • D) All of the above
QUESTION #2

• Which medications have been found to increase Dabigatran levels:
  • A) Amiodarone
  • B) Atorvastatin
  • C) Carvedilol
  • D) All of the above
QUESTION #3

• Hemodialysis is an effective means of removing the following drugs:
  • A) Direct Thrombin Inhibitor
  • B) Factor Xa inhibitors
  • C) Vitamin K antagonist
  • D) None of the above
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