REVERSAL OF ORAL ANTICOAGULATION

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AVAILABLE ORAL ANTICOAGULANTS

Direct Thrombin Inhibitors	Factor Xa Inhibitors	Vitamin K Antagonists
Dabigatran	Apixaban Betrixaban Edoxaban Rivaroxaban	Warfarin

INITIAL ASSESSMENT

- How severe is the bleeding and where is it located?
- Is the patient actively bleeding now?
- Which agent is the patient receiving?
- When was the last dose of anticoagulant administered?
- Could the patient have taken an intentional or unintentional overdose of the anticoagulant?
- Does the patient have a history of renal or hepatic disease that might cause excessive anticoagulant effect in the setting of standard drug dosing?
- Is the patient taking other medications that could affect hemostasis?
- Does the patient have other comorbidities that could promote bleeding?

ASSESSMENT OF ANTICOAGULATION STATUS

Medication	Half-life	Renal
Apixaban	8-15 hrs	25%
Betrixaban	19-27 hrs	11%
Dabigatran	12-17 hrs	80-85%
Edoxaban	6-11 hrs	35%
Rivaroxaban	5-9 hrs	35%
Warfarin	42-72 hrs (factor II)	92%

ASSESSMENT OF ANTICOAGULATION STATUS: COAGULATION TESTING

- Normal coagulation testing cannot be used as evidence that the anticoagulant effect has resolved
- Typically obtain: PT/INR and aPTT
- Thrombin clotting time (TT) or dilute TT
  - Normal TT or dilute TT = no clinically relevant dabigatran effect
- Anti-factor Xa levels
  - Must be calibrated to the drug in question
  - Absence of anti-factor Xa activity = no clinically relevant anti-factor Xa drug effect

ANTICOAGULANT REVERSAL

- A specific reversal agent
- Non-specific reversal agent
- Antifibrinolytic agent
- Drug removal from circulation and/or GI tract

ANTICOAGULANT REVERSAL: SPECIFIC AGENTS

- Idarucizumab (Praxbind) – FDA approved October 2015
  - Humanized monoclonal antibody fragment that binds specifically to dabigatran
  - **Dose**: 2.5 gm IV x 2 no more than 15 minutes apart
  - Do **NOT** combine with PCC products
  - AWP: $44.52 (2.5 gm vial)

ANTICOAGULANT REVERSAL: SPECIFIC AGENTS

- Andexanet alfa (AndexXa) – FDA approved May 2018
  - Catalytically inactive form of fa… …aban and apixaban

Drug FXa Inhibitor	…
Rivaroxaban	…3 Hours
Apixaban	…w dose
	…w dose

Black Box Warning: Treatment with andexanet alfa has been associated with serious and life-threatening adverse events, including: Arterial and venous thromboembolic events, ischemic events (including myocardial infarction and ischemic stroke), cardiac arrest, and sudden deaths. Monitor for thromboembolic events and initiate anticoagulation when medically appropriate. Monitor for symptoms and signs that precede cardiac arrest and provide treatment as needed.

  - Do **NOT** combine with PCC p…
  - AWP: $3300 (100 mg vial) and $6600 (200 mg vial)

ANTICOAGULANT REVERSAL: NON-SPECIFIC AGENTS

	Clotting Factors	Available Products	Dose	Price
3F-PCC	II, IX, X	Profilnine SD	25-50 units/kg	$1.61/unit
4F-PCC	II, VII, IX, X	K	/kg	$2.90/unit
aPCC	II, VII, IX, X	F		$2.70/unit

Black Box Warning: Both fatal and nonfatal arterial and venous thromboembolic complications have been reported with prothrombin complex concentrate in clinical trials and post marketing surveillance. Monitor patients receiving prothrombin complex concentrate for signs and symptoms of thromboembolic events

- Administer concurrently with vitamin K 10 mg IV (warfarin reversal only)
- Monitor INR at baseline and 30 minutes post-dose (warfarin reversal only)
- Unactivated PCCs and aPCCs are potentially prothrombotic

ANTICOAGULANT REVERSAL: ANTIFIBRINOLYTIC AGENTS

Medication	Dose
Epsilon-aminocaproic acid	2 gm IV Q6H 3 gm PO TID-QID
Tranexamic acid	10-20 mg/kg IV x 1 then 10 mg/kg IV Q6H-Q8H 1-1.5 gm PO Q8H-Q12H

ANTICOAGULANT REVERSAL: DRUG REMOVAL

- Oral activated charcoal
  - **Dose**: 50 gm PO/PT x 1
  - If anticoagulant administered within the previous 2 hours and patient can tolerate
- Hemodialysis
  - May be used to remove dabigatran from circulation
  - Will not remove factor Xa inhibitors or warfarin d/t high protein binding

ANTICOAGULANT REVERSAL: SUMMARY

Agent	**Dabigatran**	**Apixaban** **Betrixaban** **Edoxaban** **Rivaroxaban**	**Warfarin**
Possible Interventions	Idarucizumab 4F-PCC (if specific agent N/A) 3F-PCC +/- FFP Antifibrinolytic agent Oral activated charcoal Hemodialysis	Andexanet alfa 4F-PCC (if specific agent N/A) 3F-PCC +/- FFP Antifibrinolytic agent Oral activated charcoal	4F-PCC + vitamin K IV 3F-PCC + FFP + vitamin K IV FFP + vitamin K IV

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