Perioperative Implications

Preoperative Preparation

- Rule out associated traumatic injury.
- Hemodynamic control.
- Aspiration prophylaxis.
- Sedation if agitation is severe; benzodiazepines as first line treatment.

Monitoring

- Temperature
- Neuromuscular blockade

Airway

- Aspiration risk

Preinduction/Induction

- Salivation and N/V may justify the decision to utilize rapid sequence induction.
- Ketamine should be avoided, which may have synergic effects with LSD.
- Succinylcholine should be avoided.
- Exaggerated response to endogenous and exogenous catecholamines.

Maintenance

- Maintain normothermia.

Extubation

- At risk for aspiration.
- Continue supportive reassurance.

Adjuvants

- May have exaggerated response to sympathomimetic agents
- Potential for serotonin syndrome in pts taking concomitant serotonin precursors/agonist (SSRI, SNRI)
- Theoretical potential for ester local anesthetic toxicity due to inhibition of plasma cholinesterase activity
- Theoretical potential for prolongation of succinylcholine neuromuscular blockade due to inhibition of plasma cholinesterase activity

Anticipated Problems/Concerns

- Avoid injuries associated with agitation.
- Possible concomitant drug and/or alcohol use by pt.

Drug Overdose, Rat Poison (Warfarin Toxicity)

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Risk

- Major risk is hemorrhage, especially CNS or GI.
- Incidence: Risk of hemorrhage in 1–7.4% of pts chronically anticoagulated. Risk is dose-related and proportional to PT prolongation. Risk of hemorrhage doubles as INR increases from 2.0–2.9 to 3.0–4.4. It further quadruples as INR increases from 3.0–4.4 to 4.5–6.9. Age is associated with increased sensitivity to warfarin and increased incidence of bleeding complications.
- Rx for DVT, cerebral vessel atherosclerosis, prosthetic heart valves, mitral stenosis, and atrial fibrillation.

Perioperative Risks

- Bleeding
- Drugs that potentiate anticoagulant effects: Antibiotics (especially metronidazole, sulfonamides, cephalosporins), NSAIDs, phenytoin, cimetidine, barbiturates, alcohol

Worry About

- Bleeding complications of invasive procedures.
- Drug interactions.
- Transient protein C deficiency preceding effect on procoagulant levels at initiation of warfarin therapy leading to thrombotic complications.
- True poisoning with rodenticides (so-called superwarfarins) may result in prolonged clotting abnormality with abnormal PT values weeks to months post event because of the enormously long half-lives of these drugs.

Overview/Pharmacology

- Vitamin K antagonist.
- Cleared by hepatic and renal transformation and excretion. $T_{½}$ is approximately 40 h. Duration of action is 2–5 d.
- Onset of effect is delayed by 8–12 h because of time required to clear already synthesized clotting factors. For similar reasons, peak effect of a dose occurs 48 h post-administration.

Drug Class/Mechanism of Action/Usual Dose

- Blocks vitamin K–mediated carboxylation of factors II, VII, IX, X (procoagulants); protein C, protein S (anticoagulants).
- Carboxylation of coagulation factors oxidizes vitamin K. The vitamin K epoxide must be reduced to become active again. Coumarin anticoagulants block reduction of the epoxide. Thus large and/or repeat doses of vitamin K are needed for large overdoses or for long-acting forms.
- Chronically taken for systemic anticoagulation for DVT, CVA, prosthetic valves, and atrial fibrillation.
- Usual doses: Loading regimen varies, but maintenance dose is 2.5–10 mg/d.
- Alternatives: Other oral anticoagulation agents include the direct thrombin inhibitor, dabigatran, and the Xa inhibitors rivaroxaban and apixaban. Although these drugs all have the advantage of standardized dosing and none need lab monitoring, they also do not have established antidotes.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEME	Abnormal levels of factor II, IV, IX, X, and protein C, protein S	Easy bruising, prolonged bleeding time	Ecchymoses	PT

Key References: Holbrook A, Shulman S, Witt D, et al.: Evidence-based clinical practice guidelines: antithrombotic therapy and prevention of thrombosis, ed 9.: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines, *Chest* 141(Suppl 2):e152S–e184S, 2012; Frumkin K: Rapid reversal of warfarin-associated hemorrhage in the emergency department by prothrombin complex concentrates, *Ann Emerg Med* 62(6):616–626, 2013.

Perioperative Implications

Possible Drug Interactions: Preoperative

- Increased effect: Antibiotics, NSAIDs, oral hypoglycemic, diazepam, cimetidine, diuretics, and phenytoin.
- Decreased effect: Methylxanthines, rifampin, antihistamines, corticosteroids, and barbiturates.
- Relatively minor surgical procedures may be performed without reversal of warfarin anticoagulation.
- Major surgical procedures warrant discontinuation of drug 1–3 d preop, with a target PT within 20% of nanoliter range. If discontinued, the need for bridging with low-molecular-weight heparin prior to surgery should be considered.
- For urgent surgery, pt may be given 10–20 mL/kg of FFP and 5–10 mg of vitamin K IV, with additional amounts of both given as needed.
- For emergent surgery, life-threatening bleeding, or the pt who cannot tolerate the volume of FFP for reversal, a four-factor PCC (KCentra in USA) is approved for use by the FDA. If a four-factor PCC is not available, evidence suggests effectiveness of a three-factor PCC (Bebulin, Profilnine, or FEIBA in USA) plus rVIIa or FFP. The value of rVIIa alone to reverse warfarin is unclear because, although it can normalize INR, the correlation of INR to clinical bleeding is not defined in that setting. This is because the PT is more sensitive to levels of VII and X than II or IX, and there is insufficient literature to evaluate a clinical effect. Regardless of what means are chosen, the need for repeat dosing should be considered and vitamin K IV should also be given since the effect of warfarin greatly exceeds the half-lives of these concentrates

Possible Drug Interactions: Adjuvants/Regional Anesthesia/Reversal

- Regional block: Relatively contraindicated without reversal of anticoagulation
- Peripheral block: Relatively contraindicated without reversal of anticoagulation

Anticipated Problems/Concerns

- It should always be kept in mind that the pt is chronically anticoagulated for an underlying thrombotic condition or risk. This should be balanced against the decision to reverse anticoagulation.
- All factor concentrates carry an inherent risk of thrombosis simply by their ability to disturb the balance of procoagulant and anticoagulants. Although such products as KCentra attempt to mitigate that by including heparin, antithrombin, protein C, and protein S, this is no guarantee against pathologic thrombosis.
- Because it contains heparin, KCentra is contraindicated in pts with a history of HIT.
- Hypothermia will potentiate anticoagulant effect.