



Neuro Pharmacotherapy Pearls

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Conflicts of Interest/Disclosures: None

Pharmacotherapy

Objectives

Describe the pharmacology, pharmacokinetics and pharmacodynamic characteristics of medication used in acute stroke setting

Identify potential adverse drug effects and drug interactions for medications used in acute stroke patients

Determine the optimal pharmacotherapy strategy for a patient with acute neurological injury

Stroke Medication Review

Hyperosmolar therapy

Antithrombotic agents

**Anticoagulant reversal
and hemostatic agents**

Anti-shivering agents

**Neuromuscular
blocking agents**

**Antihypertensive
agents**

Sedation

**Vasopressor and
inotropes**

Antimicrobials



Hyperosmolar Therapy Pearls

Hyperosmolar Therapy Comparison

	Mannitol 20%	Sodium Chloride 23.4%
Equi-osmolar dose	1 gm/kg	0.687 mL/kg
Osmolarity	1098 mOsm/L	7987 mOsm/L
Infusion	IVPB over 5-15min	IV push over 10-20min
Line	Central preferred	Central
Monitoring	Osmolar Gap - trough BMP and serum osmolality Strict fluid ins/outs Electrolytes	Trough sodium levels

Hyperosmolar Therapy Case

- 55 YO male post TBI, sustained ICP 32 mmHg x 5 minutes
- Has received 1 dose of 23.4% NaCl and 1 dose of mannitol in last hour
- Lab findings:
 - Na 147 mEq/L
 - K 3.5 mEq/L
 - Cl 112 mEq/L
 - HCO₃ 17 mEq/L
- What is the best osmotic therapy for this patient for ICP control?
 - 30 ml of 23.4% NaCl
 - Mannitol at 1gm/kg

- BUN 18 mg/dL
- Cr 1.4 mg/dL
- Gluc 210 mg/dL

Mannitol Pearls



Requires in-line filter
(precipitates-crystal formation)

May require warming to dissolve
crystals before administration



May be given via peripheral access



Duration of effect 90 min – 6 hr



Monitor trough osmotic gap

Goal < 15-20 mOsm/L



Osmolar gap = Measured osmolality – Calculated osmolality



Osmolar gap = Measured osmolality – [(2 x Na) + (BUN/2.8) +
(glucose/18)]

Hypertonic Saline Pearls

Central access is required for

- 23.4% NaCl bolus
- >2% NaCl if using continuous infusion

Duration of effect 30-90 min – 4 hour

Controversial if continuous infusion is helpful for ICP control

Monitor serum sodium every 4-6 hours (trough)

- Avoid prolonged hypernatremia > 160 mEq/L

Adverse Reactions

Mannitol

- Rebound ICP elevation with abrupt discontinuation (with high, repeated dosing)
- Acute kidney injury
- Dehydration
- Hypotension
- Electrolyte imbalances

Hypertonic Saline

- Pulmonary edema
- Heart failure
- Acute kidney injury
- Coagulopathy
- Hypernatremia
- Metabolic acidosis
- Thrombophlebitis
- Osmotic demyelination syndrome



Antithrombotic Pearls



T-PA Pearls

- Swirled, not shaken
- Prepare the appropriate dose of t-PA
 - Remove excess drug from the bottle before infusion to prevent inadvertent administration of total doses of >90 mg and increased risk of intracerebral bleeding
- DOAC (Direct Oral AntiCoagulants) administration within the last 48 hours or any abnormal coagulation tests for these specific agents are a contraindication for receiving t-PA
 - Determine time of last dose if possible and renal function

Antithrombotic Considerations



Clopidogrel

30% of the population have genetic polymorphisms and do not respond to clopidogrel as it is a prodrug



DOACs

Significantly lower intracranial bleeding risk than warfarin, but are associated with a risk of gastrointestinal bleeding



ASA

If a patient is on a DOAC and needs ASA treatment, there is an increased risk of bleeding and the risk to benefit ratio must be considered until the DOAC has had time to be cleared from the body (i.e. approximately 4-5 half-lives)



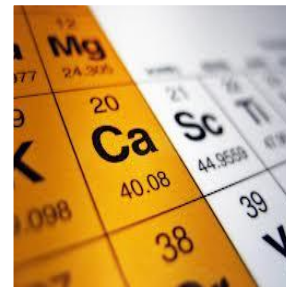
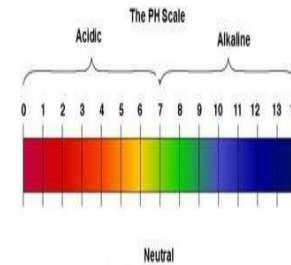
Coagulation Reversal Pearls

Optimizing the Coagulation Cascade



Normal Body
Temperature

Normal
Acid/Base Status



Electrolyte
Balance

Acute Reversal: Life- threatening bleeding

Hold	Hold anticoagulant (if receiving one)
Consider	If anticoagulant given within 2 hours, consider activated charcoal 50g
Give	Give vitamin K 10mg IV (for warfarin) <ul style="list-style-type: none">• Do not administer SQ
Consider	Consider administration of PCC or FFP
Recheck	Recheck INR 30 minutes after PCC or FFP (if appropriate based on anticoagulant)

Acute Reversal: Life- threatening bleeding

Warfarin

- For rapid reversal, guidelines suggest use of PCC agents over FFP

Dabigatran

- Idarucizumab binds dabigatran to neutralize its anticoagulant effects

Factor-Xa inhibitors

- Andexanet is now FDA approved for rivaroxaban and apixaban bleeds, whereas consider 4-factor PCC for others

PCC vs FFP

Prothrombin Complex Concentrate (PCC)

- Low Volume
- Rapid administration
- Expensive
- Risk of thrombosis risk is unknown
- 4 Factor PCC contains II, VII, IX, X and heparin

Fresh Frozen Plasma (FFP)

- Accessibility
- Inexpensive
- Large volume (15-20 mL/kg)
 - Tolerability issues for patient with cardiac/pulmonary/renal disease
- Transfusion reactions

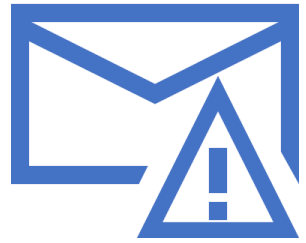
Which of the following agents will achieve the fastest reversal of laboratory parameters in a patient receiving rivaroxaban?

- Andexanet
- Vit K
- PCC
- FFP

Which factor is used to determine the dose of PCC?

- II
- VII
- IX
- X

Acute Antithrombotic Reversal Case



Neuromuscular Blocking Agents



Neuromuscular Blocking Agent

Medication	Administration pearls
Succinylcholine	<ul style="list-style-type: none">• Cannot be reversed• May cause slight increases in intracranial pressure (ICP; inconsistent data)• Severe hyperkalemia may occur in patients with burns, severe muscle trauma, neuromuscular diseases, strokes, spinal cord injury, multiple sclerosis, and prolonged immobilization• Contraindicated in patients with<ul style="list-style-type: none">• Malignant hyperthermia• Hyperkalemia (serum potassium > 5.0 mEq/L)
Pancuronium	<ul style="list-style-type: none">• Conditions that slow circulation may delay onset• Increased effect in patients with myasthenia gravis or Eaton-Lambert disease
Vecuronium	<ul style="list-style-type: none">• No significant cardiovascular effects• No effect on ICP
Cisatracurium	<ul style="list-style-type: none">• Longer half-life in elderly• Used as a continuous infusion in ICU during mechanical ventilation• Elimination via enzymatic breakdown and does not rely on renal or liver function for clearance
Rocuronium	<ul style="list-style-type: none">• Needs to be refrigerated• Prolonged duration in renal failure

Summary

Pharmacokinetic and pharmacodynamic characteristics must be considered to optimized stroke treatment strategies



Potential adverse drug effects and drug-drug interactions must be identified and considered when developing an individualized patient care plan in the acute setting of neurological injury



Questions?