Phenylephrine (Neo-Synephrine)

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Uses

- Prescribed mainly as nasal decongestant or ophthalmically for treatment of mydriasis, capillary decongestion.
- Reliable vasopressor in treatment of hypotension.
- Used in obstetric anesthesia for hypotension after spinal. More effective as a prophylactic infusion than bolus doses.
- Prolongs local anesthetic duration in regional anesthesia.
- Available as parenteral IM/IV and various ophthalmic and/or nasal preparations.

Perioperative Risks

- Risk of Htn increases left heart work; may precipitate myocardial ischemia, MI.
- Infusions to augment systolic BP incidence of myocardial ischemia in pts undergoing carotid endarterectomy.
- Increased pulm vascular resistance, right heart work.
- Bradycardia may occur (usually not severe) related to baroreceptor reflex.
- Decreased renal, splanchnic blood flow.
- Systemic absorption of topical preparations may cause Htn, headache, tremulousness, myocardial ischemia.

Worry About

- Increase preload, afterload may worsen LV failure in pts with LV dysfunction.
- Raised PA pressures may worsen RV dysfunction.
- May decrease renal blood flow.

Overview/Pharmacology

- Direct α_1-agonist activity causes systemic and PA vasoconstriction, resulting in increased impedance to forward flow, reduced BP.
- Rapidly metabolized by MAO.
- IV duration less than 5 min.
- May terminate supraventricular tachycardia by vagal reflex from baroreceptor stimulation.
- Increased SVR during CPB.
- Increased perfusion pressure to vital organs in hypovolemic pts until volume is restored, CPR.
- May be used in conjunction with nitroglycerin to elevate coronary perfusion pressure in hypotensive pts with myocardial ischemia.
- Decreasing R-to-L shunts in pts with cyanotic spells (TOF)
- Vasopressor of choice in hypertrophic cardiomyopathy, systolic anterior motion of mitral valve and aortic stenosis, when increased inotropy or tachycardia undesirable.
- Advantageous in catecholamine-depleted pts (chronic cocaine or amphetamine abuse), or in those on tricyclic antidepressants or MAO inhibitors, when indirect vasopressors are unpredictable.

Drug Class/Mechanism of Action/Usual Dose

- Synthetic noncatecholamine activates predominantly α-adrenergic receptors (postsynaptic, heart, iris), triggers release of intracellular calcium, resulting in smooth muscle contraction.
- Differs structurally from epinephrine only in lacking 4-hydroxyl group on benzene ring.
- Usual adult dosage
  - IV bolus: 50–100 μg
  - IV infusion: 20–200 μg/min
  - Ophthalmic solutions: 2.5–10%
  - Supraventricular tachycardia dose: 150–800 μg titrated to raise BP

Assessment Points

System	Effect	PE	Test
HEENT	Mydriasis without cycloplegia Increased production of aqueous humor		
CV	Vasoconstriction of veins and arteries Increased systolic and diastolic BP Decreased HR	BP HR	PCWP ECG
RESP	Increased PVR		PCWP, PAP
RENAL	Increased renal blood flow	UO	BUN, Cr

Key References: Dellinger RP, Levy MM, Carlet JM, et al.: Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2008, *Intensive Care Med* 34(1):17–60, 2008; Habib AS: A review of the impact of phenylephrine administration on maternal hemodynamics and maternal and neonatal outcomes in women undergoing cesarean delivery under spinal anesthesia. *Anesth Anal* 114(2):377-390, 2012.

Perioperative Implications

Preoperative Concerns

- Assess LV function and Hx of CAD.
- Consider arterial catheter if phenylephrine infusion anticipated (carotid endarterectomy, relative hypovolemia).
- Assess renal function (Cr).
- For nasal intubations, phenylephrine can be used as a nasal vasoconstrictor in a mixture with 3–4% lidocaine.

Induction/Maintenance

- Monitor ECG for signs of ischemia due to increased ventricular work or coronary artery spasm.
- May decrease hepatic blood flow due to α-adrenergic–mediated vasoconstriction of portal venous vasculature.

Adjuvants/Regional Anesthesia/Reversal

- Duration may be prolonged in pts on MAO inhibitors.
- Side effects with ophthalmic use occur within 20 min; usually self-limited.
- 2.5% nasal, ophthalmic solutions recommended in infant and elderly populations or in pts with CAD.

Anticipated Problems/Concerns

- Can be titrated slowly to avoid overshoot (with resultant Htn).
- Can be used when severe hypotension presents immediate danger to compromised myocardium or other end organ (e.g., brain).
- With a failing heart, increasing afterload and preload may increase left-sided filling pressures enough to precipitate pulm edema.

Phenytoin

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Uses

- Management of generalized tonic-clonic (grand mal) and complex partial seizures
- Prophylaxis against seizures after trauma or surgical intervention
- Treatment of ventricular arrhythmias, especially those associated with digitalis or tricyclic antidepressant toxicity
- Treatment of prolonged QT interval
- Treatment of epidermolysis bullosa and chronic pain syndromes

Overview/Pharmacology

- Drug of choice for status epilepticus
- Treatment for acute and chronic seizures
- Onset of action: 30–60 min
- Protein binding >90% in adults
- Elimination half-life: 22 h
- 95% hydroxylated and conjugated in liver with glucuronic acid for renal excretion
- Therapeutic range: 10–20 μg/mL

Drug Class/Mechanism of Action/Usual Dose

- Hydantoin derivative
- In the CNS, helps to limit nerve impulse generation, thereby limiting spread of seizure focus by:
  - Decreasing influx of Na^+ ions across cell membranes in the motor cortex
  - Decreasing presynaptic Ca^{2+} release
  - Decreasing extracellular K^+ concentration
- In the heart, works to limit reentrant arrhythmias by:
  - Prolonging the effective refractory period and suppressing ventricular pacemaker automaticity
  - Shortening the action potential for status epilepticus (IV and PO dosages are the same)
- Pediatric: Loading dose, 15–20 mg/kg in single or divided doses, then 5 mg/kg per d in divided doses
- Adult: Loading dose, 10–15 mg/kg, then 5–6 mg/kg per d in 3 divided doses
- For treatment of cardiac arrhythmias: 1.5 mg/kg IV every 5 min for maximum dose of 15 mg/kg or 1.5 g