Vasopressors and Inotropes

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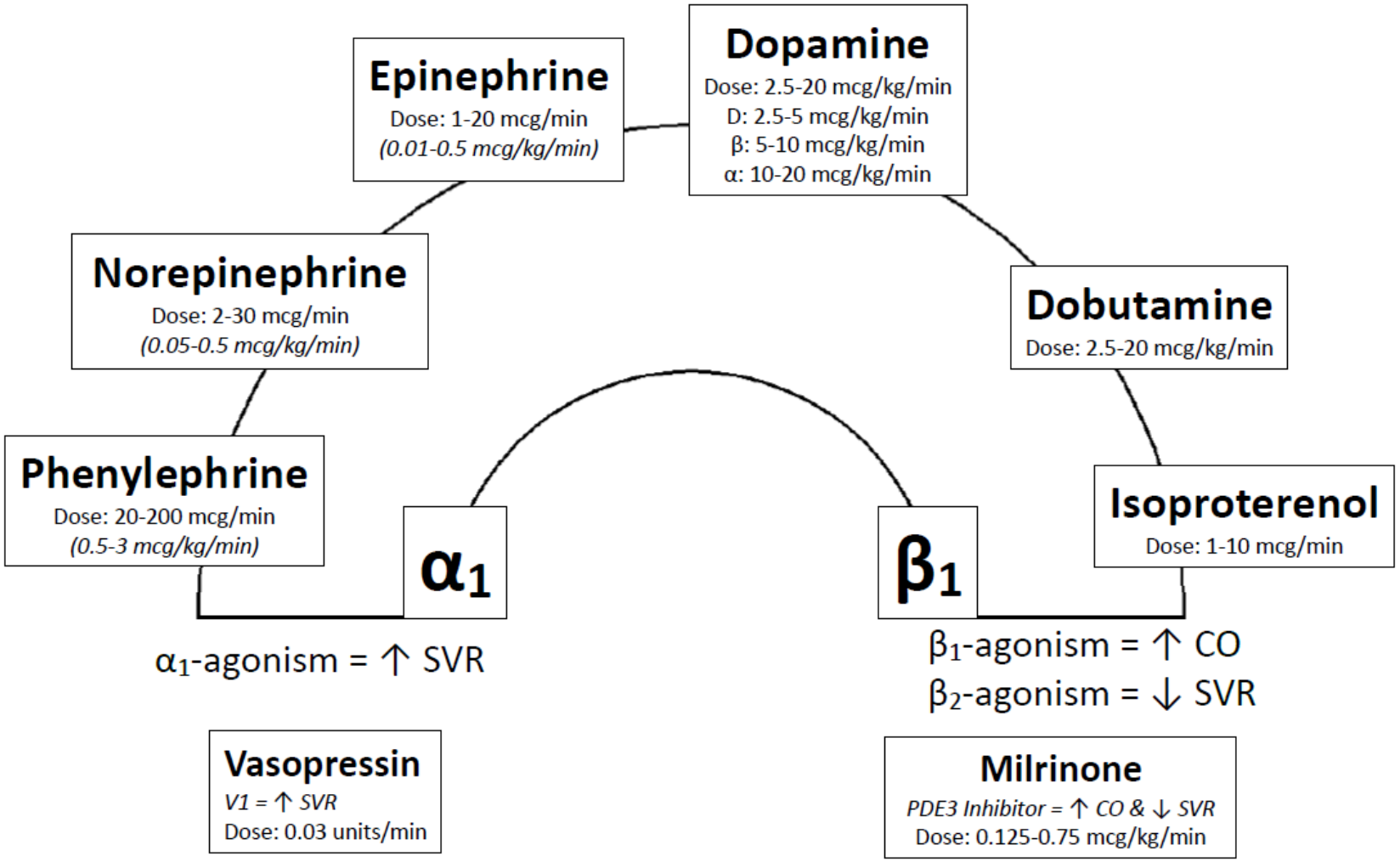
Adrenergic Receptors

Receptor	Location	Action	Effect
α1 *Vasopressors*	Systemic Vasculature	Vasoconstriction	↑ SVR
β1 *Inotropes*	Myocardium	↑HR ↑contractility	↑ CO
β2 *Vasodilators*	Systemic Vasculature	Vasodilation	↓ SVR

Vasopressors and Inotropes



Norepinephrine (Levophed®)

- Potent α effects with moderate β
  - Primary: Vasoconstriction = ↑SVR
  - Secondary: ↑cardiac contractility & HR = ↑ CO
- Dose
  - 2-30 mcg/min
  - *0.05-0.5 mcg/kg/min*
- Clinical Use
  - Clear drug of choice for septic shock
    - Mortality benefit demonstrated over Dopamine
  - Suggested drug of choice for undifferentiated and cardiogenic shock
- Notes
  - Potential rate limiting tachycardia/tachyarrythmias

Phenylephrine (Neosynephrine®)

- Pure α agonist
  - Vasoconstriction = ↑ SVR
    - Unopposed α effects can lead to significant ischemia
- Dose
  - 20-200 mcg/min
  - Bolus dose: 100-200 mcg Q 3-5 min
- Clinical Use
  - Septic shock in patients who do not tolerate norepinephrine
  - Anesthetic induced hypotension
  - Shock in patients with Aortic/Mitral Stenosis
- Notes
  - Least arrythmogenic
    - Potential for reflex bradycardia

Vasopressin (Vasostrict®)

- Vasopressin receptors
  - V_1→ Vasoconstricts vascular smooth muscle = ↑ SVR
  - V_2 → Reabsorbs H_20 from renal collecting duct = ↓ UOP
- Dose
  - 0.03 units/min
- Clinical Use
  - Adjunct to Norepinephrine in refractory shock
    - Does not provide morbidity/mortality benefit
    - Reduces Norepinephrine requirement
  - Patients with Aortic/Mitral Stenosis
  - Patients with Pulmonary Hypertension
  - Patients with GI Hemorrhage
- Notes
  - Preserved effect in severe acidosis
  - Not arrythmogenic

Epinephrine (Adrenalin®)

- Potent α and β activity
  - Vasoconstriction = ↑ SVR
  - ↑ contractility & HR = ↑ CO
- Dose
  - 1-20 mcg/min
  - *0.01 - 0.5 mcg/kg/min*
- Clinical Use
  - Refractory shock, adjunct 2nd or 3rd line agent
    - May consider in patients with cardiogenic shock component
  - Drug of choice in anaphylaxis
    - Dose: 0.3 mg IM – Use 1 mg/1 mL vial (or EpiPen®)
  - Cardiac arrest
    - Dose 1 mg IV – Use 1 mg/10 mL emergency syringe
- Notes
  - Increased arrythmogenicity
  - May cause significant hyperglycemia and lactatemia
    - Inhibition of insulin secretion
    - Promotion of glycogenolysis and inhibition of glycogen production

Dopamine (Inotropin®)

- Dose dependent effect
  - D (2.5-5 mcg/kg/min): ↑ renal blood flow and UOP
    - No effect on rates of renal impairment or recovery
  - β (5-10 mcg/kg/min): ↑ contractility & HR = ↑ CO
  - α (10-20 mcg/kg/min): Vasoconstriction = ↑ SVR
  - Unclear relationship in clinical practice
    - Titrate according to patient response
- Clinical Use
  - Mostly fallen out of favor
  - ACLS Guidelines for management of symptomatic bradycardia as an alternative to pacing
- Notes
  - High arrythmogenicity
    - ↑ myocardial oxygen demand

Dobutamine (Dobutrex®)

- Potent β_1 & β_2 with minimal α activity
  - ↑ contractility & HR = ↑ CO
  - Systemic vasodilation = ↓ SVR
- Dose
  - 2.5 -20 mcg/kg/min
    - Usual inotropic range: 5-10 mcg/kg/min
- Clinical Use
  - Shock with ↓ CO
  - Patients with decompensated HF
- Notes
  - May cause hypotension
    - Start with low doses and titrate up
    - If patient is hypotensive consider starting vasopressor (norepinephrine) first
  - High arrythmogenicity
    - Highest with doses > 10 mcg/kg/min
  - Increases myocardial oxygen demand

Milrinone (Primcor®)

- Phosphodiesterase-3 inhibitor
  - Increased intracellular cAMP → activation of calcium channels
  - ↑ contractility & HR = ↑ CO
  - Systemic vasodilation = ↓ SVR
- Dose
  - Loading Dose: 50 mcg/kg over 10 minutes
    - Not Recommended
  - 0.125- 0.75 mcg/kg/min
- Clinical Use
  - Shock with ↓ CO
  - Patients with decompensated HF
- Notes
  - Renal Elimination; Half-life of 2-3 hours
    - Hard to titrate for acutely unstable patients
  - May cause hypotension
    - Start with low doses and titrate up
    - If patient is hypotensive consider starting vasopressor (norepinephrine) first
  - High arrythmogenicity
    - Highest with doses > 0.5 mcg/kg/min
  - Increases myocardial oxygen demand

Isoproterenol (Isuprel®)

- Pure β agonist
  - ↑ contractility & HR = ↑ CO
  - Systemic vasodilation = ↓ SVR
- Dose
  - 1-10 mcg/min
- Clinical Use
  - Bradyarrhythmias, Heart Block, and Torsade de Pointes
- Notes
  - Generally restricted to Cardiology

Administration of Vasopressors

- Peripheral administration not recommended due to risk of infiltration and extravasation injury
- If no central access available, appropriate to start vasopressors peripherally
  - Short term peripheral use has been found to be of minimal risk
  - Use largest peripheral IV site possible
  - Use least concentrated formulation of whichever agent is most appropriate based on patient scenario
- Once patient stabilized, work to obtain central access
  - Ideally within 6-12 hours of starting vasopressors

Management of Extravasation

- Extravasation of vasopressors can result in severe ischemic injury and tissue necrosis
- In the event of extravasation, antidotes are available:
  - Phentolamine: α-blocker
    - Drug of choice
    - 5-10 mg diluted in 10 mL flush
    - Inject locally in affected area
  - Terbutaline: β-agonist
    - Use only if phentolamine unavailable
    - 1-2 mg diluted in 10 mL flush
    - Inject locally in affected area
  - Nitroglycerin ointment
    - Described for mild extravasation injuries
    - Apply to affected area

Key Points

- Ongoing assessment of fluid status and maintaining euvolemia is critical
- Hypoxia and acidemia may blunt effects of catecholamine vasopressors and inotropes
  - Vasopressin's effects are preserved
- Hypocalcemia may lead to inadequate response
  - Replete patients with hypocalcemia
  - Consider empiric calcium in patients receiving multiple blood transfusions

Questions