Vasopressors and Inotropes

Outline
- Principals of Use for Vasopressors and Inotropes
- Adrenergic Receptor Review
- Vasopressors
- Inotropes

Case Presentation
- 68 YOM with CC of weakness and fever
- Vitals: T 39.1 RR 24 HR 108 PO2 95% BP 80/50
- CXR: Bilateral infiltrates; EKG Sinus Tach
- Medications given in ED
  - 2L of 0.9% NS
  - Acetaminophen 650mg supp
  - Ceftriaxone and Azithromycin
- Vitals: T 38 RR 26 HR 120 PO2 93% BP 70/40
- What to do next?

Indications for Vasopressors
- Hypotension may result from:
  - Hypovolemia
  - Cardiogenic
  - Distributive

- Vasopressors are indicated for:
  - SBP decrease of 30mmHg from baseline or
  - MAP <60 mmHg and
  - Evidence of organ dysfunction due to hypoperfusion

- Hypovolemia must be corrected first

Vasopressors and Inotropes
- What is the difference between a vasopressor and an inotrope?
- Vasopressors induce vasoconstriction and thereby increase mean arterial pressure (MAP)
- Inotropes increase cardiac contractility

Principles of Use for Vasopressors and Inotropes
- Use of vasopressors and inotropes is guided by three fundamental concepts:
  - One drug, many receptors
  - Dose–response curve
  - Direct versus reflex actions

- Central venous catheter preferred
Principles of Use for Vasopressors and Inotropes

- Choice of an initial agent should be based upon the suspected underlying etiology of shock.
- Dose should be titrated up to achieve effective BP or end-organ perfusion.
- If maximal doses of a first agent are inadequate, then a second drug should be added to the first.
- Doses must be constantly titrated to adjust for tachyphylaxis and for changes in the patients clinical condition.

Volume Resuscitation

- Repletion of adequate intravascular volume, when time permits, is crucial prior to the initiation of vasopressors.
  - Vasopressors will be ineffective or only partially effective in the setting of coexisting hypovolemia.
- Fluids may be withheld in patients with significant pulmonary edema due to ARDS or CHF.

Vasopressors and Inotropes

- Receptor Physiology
  - Categories of receptors include
    - Alpha₁ adrenergic receptors
    - Beta₂ adrenergic receptors
    - Dopamine receptors

Alpha₁ Adrenergic Receptors

- Alpha₁ receptors are located in the vascular walls
  - Activation of these receptors leads to significant vasoconstriction
  - Are also present in the heart and can increase duration of contraction without increased chronotropic effects (clinical significance uncertain)

Beta–Adrenergic receptors

- Beta₁ receptors are located primarily in the heart
  - Activation of these receptors mediates increases in inotropic and chronotropic effects
- Beta₂ receptors are located primarily in blood vessels and lungs
  - Activation of these receptors leads to vasodilation and bronchodilation

Dopamine Receptors

- Dopamine receptors are present in the renal, mesenteric, coronary, and cerebral vascular beds.
  - Stimulation of these receptors induces vasodilation
**Receptor Physiology Review**

<table>
<thead>
<tr>
<th></th>
<th>Vasodilation</th>
<th>Vasoconstriction</th>
<th>Inotropic</th>
<th>Chronotropic</th>
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<tr>
<td>Alpha</td>
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<td>Dopamine</td>
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**Differentiating Shock States**

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<thead>
<tr>
<th>Shock state</th>
<th>PCWP</th>
<th>SVR</th>
<th>CI</th>
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<tr>
<td>Alcohol</td>
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<tr>
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<td>Cardiogenic</td>
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**Adrenergic Agents**

- Dopamine (Intropin®)
- Norepinephrine (Levophed®)
- Phenylephrine (Neosynephrine®)
- Epinephrine (Adrenaline®)

**Dopamine**

- Onset of Action: 5 Minutes
- Half-life: 2 Minutes
- Duration of Action: 10 minutes
  - If used in patients on MAO inhibitors, duration of action can be greater than 1 hour
  - 50% action due to ↑ in NE
- Wide inter-patient variability

**Dopamine**

- At 1–3 mcg/kg/min, it primarily activates the dopamine receptors
  - The “renal-dose” dopamine effect
- At 5–10 mcg/kg/min, it works primarily on Beta-1 receptors
  - Increased cardiac output
- At greater than 10 mcg/kg/min, it works primarily on alpha-receptors
  - Vasoconstriction

**Dopamine**

- Side Effects:
  - Splanchnic and gastric mucosal blood flow
  - Tachycardia
  - Atrial and Ventricular arrhythmias, especially at higher doses
**Norepinephrine**

- **Receptor Physiology**
  - Acts on both Alpha and beta, receptors
  - Potent vasoconstriction and less pronounced increase in cardiac output
  - Reflex bradycardia usually occurs in response to increased MAP, thus the mild chronotropic effect is canceled out.
  - Most commonly used to treat septic shock

**Onset of Action:**
- 1–2 Minutes

**Duration of Action:**
- 1–2 Minutes

**Titrate every 5–10 minutes**

- More potent than dopamine
- Dosing range of 2–30mcg/min

**Side Effects:**
- Slight ↓ in CI d/t ↑SVR
  - Although elevated SVR means increased cardiac afterload, studies show cardiac output is maintained in patients without pre-existing cardiac dysfunction.
- Vasoconstriction (elevated SVR)
  - Reflex bradycardia usually occurs in response to increased MAP, thus the mild chronotropic effect is canceled out.
  - No direct cardiac effects

**Phenylephrine**

- **Receptor Physiology**
  - Purely alpha-adrenergic activity
  - Vasoconstriction (elevated SVR)
  - No direct cardiac effects
  - Although elevated SVR means increased cardiac afterload, studies show cardiac output is maintained in patients without pre-existing cardiac dysfunction.

- **Onset of Action:**
  - 10–15 minutes

- **Duration of Action:**
  - 15 minutes

- **T1/2~ 3 hrs**
- Less potent vasoconstrictor than norepinephrine
- Dosing range 25–300mcg/min

- **Side Effects**
  - Reflex bradycardia secondary to peripheral vasoconstriction
  - Pulmonary edema

- **Ventricular arrhythmias**
**Phenylephrine**
- Indications for use:
  - Septic Shock
  - Can be effective in restoring perfusion in patients with septic shock refractory to dopamine & dobutamine.
  - May be a good selection for patients with tachyarrhythmias
  - Neurogenic Shock
  - Therapy of choice (based on underlying cause being low SVR)
  - Anesthesia induced hypotension

**Epinephrine**
- Receptor physiology
  - Potent beta1, adrenergic activity
  - Inotropic & chronotropic effects
  - Moderate Alpha and Beta2, activity
    - In low doses, alpha and beta, activity cancel each other out.
    - At higher doses, alpha-adrenergic effects predominate, producing elevated SVR along with increased cardiac activity

**Epinephrine**
- Onset of Action:
  - Rapid - 10-30 seconds
- Duration of action:
  - Less than 5 minutes
- Does cross the placenta and enter fetal circulation

**Epinephrine**
- Side Effects
  - Epinephrine infusion is associated with
    - increased myocardial oxygen consumption
    - increased systemic lactate concentrations
    - effects short-lived
    - No evidence of long-term effects
    - decreased splanchnic blood flow.

**Epinephrine**
- Indications for use:
  - Anaphylactic shock
  - primary agent
  - Septic shock
  - only used in patients unresponsive to all other pressors
  - Cardiogenic Shock
  - In patients with transplanted hearts due to denervation (no neuronal re-uptake)

**Extravasation**
- Image of extravasation on hand
**Phentolamine**
- Alpha blocker – vasodilation
- Useful to prevent tissue necrosis from alpha vasoconstrictor extravasation
  - 5mg phentolamine + 9ml sodium chloride
  - Give 1ml thru IV and then pull catheter
  - 0.25ml around the site with a TB needle
  - Elevate arm and apply warm pad

**Inotropic agents**
- Dopamine
- Dobutamine
- Milrinone

**Dobutamine**
- Receptor Physiology
  - Predominant Beta-1 receptor effect
  - increased inotropic and chronotropic effects
  - Beta-2 receptor effect
    - vasodilation (hypotension), bronchodilation
  - Net effect is increased cardiac output, with a small reduction in blood pressure

**Dobutamine**
- Onset of Action:
  - 2 Minutes, although peak effect often does not occur for up to 10 minutes
- Half-Life:
  - 2 Minutes
- No adjustments in dosage due to liver or renal disease
- Dose 2.5–20 mcg/kg/min

**Side Effects:**
- Tachycardia, arrhythmias, hypotension
- Nausea, Headache
- Does contain sodium bisulfite, and may cause allergic reactions in susceptible individuals
  - Sulfite allergies much less common than sulfate allergies

**Milrinone**
- Phosphodiesterase inhibitor
- Inotropic and vasodilatory actions
  - In many ways similar to dobutamine
  - much more expensive
  - Lower incidence of arrhythmias
  - Used in medically refractory CHF but vasodilatory properties limit use in hypotensive patients
  - Useful in patients to be continued on beta-blockers
**Milrinone**

- Onset of action 5–15 minutes
- Dosing
  - Load (optional) 50mcg/kg IV over 10 minutes
  - Maintenance infusion of 0.375–0.75mcg/kg/min
- Dose reduction for renal insufficiency
- Side effects
  - Hypotension
  - Arrhythmias
  - Hypokalemia

**Vasopressin**

- Antidiuretic hormone
- Catecholamine sparing effect in late septic shock
- Useful in combination with NE, Epi, or DA
- ACLS pulseless arrest algorithm

**Ideal Vasopressor**

- Maintain effective circulatory volume and renal blood flow
- Increase cardiac contractility
- Void of effects on HR
- Does not increase arrhythmia risks
- Tachyphylaxis is not a concern

**Choice of Vasopressor**

- Cardiogenic shock
  - Dobutamine / Norepinephrine
  - Dopamine
- Distributive
  - Septic
    - Norepinephrine
    - Dopamine
- Anaphylactic
  - Epinephrine