

---

# Vasopressors and inotropes

Finot Debebe, MD, Emergency physician



Global Health  
Emergency Medicine

# Objectives

---

- To know the different types of vasopressors and inotropes
- To reasonably select vasopressors in different clinical scenarios
- To determine the different indications and adverse effects of vasopressors



# Background

---

- ❑ Vasopressors are class of drugs that elevate Mean Arterial Pressure (MAP) by inducing vasoconstriction.
- ❑ Inotropes increase cardiac contractility.



# Receptor Physiology

---

- Main categories of adrenergic receptors relevant to vasopressor activity:
  - Alpha-1 adrenergic receptor
  - Beta-1, Beta-2 adrenergic receptors
  - Dopamine receptors



| <b>Receptor Physiology</b> |         |                         |  |
|----------------------------|---------|-------------------------|--|
| <i>Receptor</i>            |         | <i>Location</i>         | <i>Effect</i>  |
| Alpha-1 Adrenergic         |         | Vascular wall           | Vasoconstriction   |
|                            |         | Heart                   | Increase duration of contraction without increased chronotropy |
| Beta Adrenergic            | Beta-1  | Heart                   | ↑ Inotropy and chronotropy                                     |
|                            | Beta-2  | Blood vessels           | Vasodilation   |
| Dopamine                   |         | Renal                   | Vasodilation   |
|                            |         | Splanchnic (mesenteric) |  |
|                            |         | Coronary                |  |
|                            |         | Cerebral                |  |
|                            | Subtype |                         | Vasoconstriction   |

# Dobutamine

---

- Synthetic catecholamine
- Used in severe, decompensated heart failure.



# Actions

---

- Potent  $\beta_1$ -receptor agonist and a weak  $\beta_2$ -receptor agonist
- The  $\beta_1$  stimulation :- + inotropic and chronotropic effects with increase in both cardiac work and myocardial O<sub>2</sub> consumption



# Actions.....

---

- The  $\beta_2$  stimulation produces peripheral vasodilatation
- The arterial BP usually remains unchanged
- *Tends to cause pulmonary vasodilation*





# Clinical use

---

- Used in decompensated heart failure due to systolic dysfunction with normal blood pressure.
- Effective in both right-sided and left-sided heart failure.



# Dosage and administration

---

- Available in 250-mg/20ml vials
- The usual dose range is 2 to 20 $\mu$ g/kg/min
- The response can be variable in critically ill patients and elderly



# Incompatibility

---

- An alkaline pH inactivates catecholamines
  - E.g Sodium bicarbonate
- Phenytoin, magnesium sulphate, digoxin, insulin, calcium gluconate.....



# Adverse effects

---

- Tachycardia
- Ventricular ectopic beats
- Nausea
- Headache
- Hypertension



# Contraindications

---

- Hypertrophic cardiomyopathy
- History of malignant ventricular tachyarrhythmias
- Hypersensitivity



# Dopamine

---



- Endogenous catecholamine
- Serves as both a neurotransmitter and a precursor for norepinephrine synthesis.
- Activates a variety of receptors in a dose-dependent manner.



# Actions at low doses (3-5 $\mu\text{g}/\text{kg}/\text{min}$ )

---

- Selectively activates dopamine-specific receptors
- Increased blood flow in the renal and splanchnic circulations
- Also increases urinary sodium excretion (natriuresis).



## Actions at intermediate doses (5 to 10 $\mu$ g/kg/min)

---

- Stimulates  $\beta$ -receptors
- Increase in myocardial contractility
- Increase in heart rate and peripheral vasodilatation
- The contractile response to dopamine is modest compared to dobutamine.





# Actions at high doses ( $> 10 \mu\text{g/kg/min}$ )

---

- Produces a progressive activation of  $\alpha$ -receptors
- Progressive pulmonary and systemic vasoconstriction
- There is a dose-dependent increase in the wedge pressure



# Clinical Uses

---

- *Used in cardiogenic and septic shock*
- *Agent of choice in patients with cardiogenic shock and SBP between 70–90 mmHg*
- *Low dose dopamine is NOT recommended for the prevention or reversal of acute renal failure in the ICU*



# Dosage and Administration

---

- Preparation : 40 mg or 80 mg dopamine HCl per mL
- Infusions should always be delivered into large, central veins.



# Incompatibilities

---

- Inactivated by an alkaline pH
- Penicillin, ampicillin, metronidazole....



# Nor-epinephrine

---

- Powerful inotropic
  - Cardiac  $\alpha$  and  $\beta_1$  adrenoreceptors
- Peripheral vasoconstriction
  - $\alpha$  adrenoreceptors
- Dose at 2-20  $\mu\text{g}/\text{min}$



# Actions

---

- Stimulates alpha receptors and produces a dose-dependent increase in systemic vascular resistance
- Can also stimulate cardiac  $\beta$ -receptors over a wide range with variable effects on cardiac output



# Clinical uses

---

- Traditionally used as the last measure for cases of hypotension
- Vasopressor of choice in septic shock
- Cardiogenic shock
- Do not improve survival in shock states, including septic shock



# Dosage and Administration

---

Take 1 vial (4 mg) of norepinephrine

– Dilute in a 250 mL normal saline bag à 16  $\mu\text{g}/\text{mL}$  –

– Titrate to blood pressure

■ Dose at 2-20  $\mu\text{g}/\text{min}$





# Incompatibilities

---

- inactivated at an alkaline pH
- Aminophylline, pentobarbital, atropine, diazepam....



# Adverse effects

---

- local tissue necrosis from drug extravasation
- Intense systemic vasoconstriction with worsening organ function
- Arrhythmia in large doses
- Allergic reaction to sulphite



# Epinephrine

---

- 1<sup>st</sup> line in anaphylactic shock
- Stimulates  $\alpha$ ,  $\beta_1$  and  $\beta_2$  receptors
- Increases in myocardial contractility more pronounced than other inotropes



# Dosing

---

- More potent than dopamine or dobutamine
- 1 mg in 250ml of DW
- 0.02  $\mu\text{g}/\text{kg}/\text{min}$  (0-20  $\mu\text{g}/\text{min}$ )
- *Route: IV, SC, IM*



# Adverse effects

---

- May cause effects of impaired myocardial perfusion especially in patients with CAD
  - Chest pain, arrhythmias, ST depression



# Phenylephrin

---

- A pure  $\alpha$ -1 agonist.
- Potent vasoconstrictor
- It may be useful in the management of vasomotor collapse, as in distributive or neurogenic shock, also used in septic shock



# Dosing

---

- Preparation; 10mg/ml
- Can be given peripherally
- *Route: IV*
- *Dosage: 15 mg dissolved in 250 mL D5W (60 µg/mL); start at 20–30 µg/min, titrate to desired BP (0.25-4 µg/kg/min)*



# Isoproterenol

---

- Is a potent  $\beta$  agonist
- Increase in HR and myocardial O<sub>2</sub> consumption.
- *Route: IV, SC, PO, inhaled*
- *Dosage: Infusion 1–10  $\mu\text{g}/\text{min}$*





# Phosphodiesterase Inhibitors

---

- Preparation; 10mg/ml
- Can be given peripherally
- *Route: IV*
- *Dosage: 15 mg dissolved in 250 mL D5W (60  $\mu\text{g/mL}$ ); start at 20–30  $\mu\text{g/min}$ , titrate to desired BP*



# Vasopressin

---

- An endogenous peptide hormone
- Has vasoconstrictive and antidiuretic effects via receptors in the vascular smooth muscle and the kidneys.
- Usually used in diabetes insipidus or esophageal variceal bleeding
- Active on alpha receptors
- Can cause limb ischemia



# Vasopressin

---

- Shown to be useful in treatment of refractory septic shock especially as a second agent
- Effective in reversing vasodilatory shock when added to nor epinephrine
- Dose at 0.04 U/min up to 3.2 units/hr
- May cause coronary and mesenteric ischemia, hyponatremia and pulmonary vasoconstriction



# Digitalis (Digoxin)

---

- Slows conduction through A-V node and increases force of contraction
- Used in CHF and chronic atrial fib/flutter
- Can be given orally or IV

## Side effects:

- Arrhythmias
- N & V, diarrhea
- Agitation



**Table 5.4** Receptor affinity and hemodynamic effects

|                | $\alpha$ -1 <sup>a</sup> | $\beta$ -1 <sup>b</sup> | $\beta$ -1 <sup>c</sup> | $\beta$ -2 <sup>d</sup> |
|----------------|--------------------------|-------------------------|-------------------------|-------------------------|
| Dopamine       |                          |                         |                         |                         |
| Low dose       | 0                        | 2+                      | 2+                      | 2+                      |
| High dose      | 3+                       | 2+                      | 2+                      | 2+ <sup>e</sup>         |
| Dobutamine     |                          |                         |                         |                         |
| Low dose       | 0                        | 4+                      | 1+                      | 1-2+                    |
| High dose      | 1-2+                     | 4+                      | 1+                      | 1-2+                    |
| Norepinephrine | 4+                       | 2+                      | 2+                      | 0                       |
| Epinephrine    | 4+                       | 4+                      | 4+                      | 3+                      |
| Phenylephrine  | 4+                       | 0                       | 0                       | 0                       |

# Vasopressors: Principles

- Always maximize fluid administration
- Can give boluses of vasopressors (phenylephrine or ephedrine) to temporarily improve BP
- Complete assessment (while BP is better)