Inotropes and Vasopressors

Introduction

• Heart is a vital organ that pumps blood (= generate flow) to vascular beds which regulate blood pressure to perfuse tissues.

• Shock is a clinical syndrome of various causes that results in inadequate global tissue perfusion. Usually has hypotension, lead to a vicious cycle, multiple organ failure and death.

• S&S of hypoperfusion include confusion, agitation, ↓urine, tachypnea, tachycardia, lactic acidosis.

Type of Shock[d] - example causes	Volume - Preload[a]	CO[b]	SVR - Afterload[c]
Hypovolemic shock - Bleeding, fluid lost, internal vs. external	↓↓↓	~↑	↑
Cardiogenic shock - AMI, Acute HF, PE	↑	↓↓↓	↑
Distributive shock - Septic, toxic, anaphylaxis	~↓	~↑	↓↓↓

[a] S&S of ↓ preload: ↓skin turgor, dry tongue/oral mucosa, orthostatic hypotension

[a] S&S of ↑ preload: ↑JVP, edema, ascites, crackles, MR murmurs

[b] S&S of ↓ CO: ↑HR, ↓pulse pressure

[c] S&S of ↓ afterload: warm skin

[c] S&S of ↑ afterload: cool, clammy, mottled skin, ↓cap refills

[d] Other types of shock: hypoadrenal, neurogenic, obstructive

Inotrope and vasopressor drugs (circ 2008:118:1047. Drug information handbook 2012)

• "Pick the right poison" – Limited adequate RCT. Use as minimal as needed.

• Choice of treatment is based on hemodynamic effects:

α-1 adrenergic stimulation: Induces vasoconstriction.

β-1 adrenergic stimulation: ↑Inotropy (↑contractility), ↑chronotropy (↑tachycardia).

β-2 adrenergic stimulation: Induces vasodilation.

Dopaminergic receptor: Selective vasodilator for renal, mesenteric, coronary, and cerebral vascular beds and inducing norepinephrine release.

• Overall CO, HR and BP effects may not be as described as mechanisms of action due to reflexive autonomic and physiologic changes e.g. medication that is vasodilator may not ↓BP because of reflexive ↑stroke volume.

• Inotropes: Dobutamine, Milrinone, Levosimendan

• Vasopressors: Epinephrine, Norepinephrine, Dopamine, Vasopressin, Phenylephrine

	Action	**Usual dose**	**Contra ctility[1]**	**After load[2]**	**Note**
Epinephrine	α1 **β1** β2	0.01 - 0.1 mcg/kg/min	↑↑↑↑	↑↑↑	• At low dose = more β, like dobutamine • At high dose = more α, like norepi • Use: ACLS, anaphylaxis • S/E: Splanchnic vasoconstriction
Norepinephrine Levophed)	**α1** β1 β2	0.01 - 3 mcg/kg/min	↑↑↑	↑↑↑↑	• Potent vasoconstriction • Moderate ↑CO with ~ HR effect (reflex bradycardia from increased afterload • Use: Septic shock
Dopamine Low Moderate High	DA α1 **β1** **β2** DA **α1** **β1** β2	0.5 - 2 mcg/kg/min 2 - 10 mcg/kg/min 10 - 20 mcg/kg/min	~ ↑↑ ↑↑	↓ ↑ ↑↑↑	• Precursor to norepi but more β effect • Dose-dependent effects • Dose is varied pt to pt • Use: Septic shock, 2nd-line alternative to norepinephrine
Dobutamine	β1 β2 (α1)	2 - 20 mcg/kg/min	↑↑	↓↓	• Not a vasopressor • Inotrope with a vasodilation • ↑CO + ↓SVR, may not ↓ BP • Use: HF, cardiogenic shock
Milrinone	PDE3 inh	0.375 - 0.75 mcg/kg/min	↑↑	↓↓↓	• Similar to dobutamine but more vasodilator and ↓PA • Use: HF, cardiogenic, RV failure
Isoproterenol	β1 β2	2 - 10 mcg/min	↑	↓↓↓	• Prominent chronotropic • Prominent vasodilation • Use: Bradycardia
Phenylephrine (Neo-Synephrine)	α1	0.5 - 10 mcg/kg/min	0	↑↑↑	• Pure vasoconstriction • May decrease SV
Vasopressin	V_1	0.04 unit/min	0	↑↑↑	• Pure vasoconstriction. • Use: 2nd- line in refractory distributive shock • S/E: Coronary, mesenteric ischemia, skin necrosis. ↓Na and pulm vasoconstriction
Levosimandan	Calcium sensitizer and vasodilator	Loading: 12 mcg/kg then 0.05 - 0.2 mcg/kg/min	↑↑	↓↓	Not approved in the US. Approve in Thailand in 2016

Clinical points for treating patients with shock

• A patient may simultaneously have various types and causes of shock.

• Goals of treatment are to promptly resuscitate, promote end-organ recovery and treat the cause of shock.

• The diagnosis of the cause of shock should not delay the treatment of shock.

• Replace fluid as needed with crystalloid (nejm 2004;350:2247).

• Inotropes and vasopressor should be given via central venous line to ↓risk of peripheral extravasation.

• All inotropes share the same S/E of ↓BP (if too much vasodilatation), ↓perfusion (if severe vasoconstrict), arrhythmia (AF, VT/VF), myocardial ischemia (from ↑ MVO2), hyperglycemia.

• PA catheter can help ddx type of shock but have not shown to improve outcomes when use routinely in patient with shock.

• If PA cath is used, tailored therapy to target MAP > 50-60, CVP 8-12, PCWP <18, SVR ~800, CI >2.5, Mixed venous O2Sat >70%.

• Consider invasive continuous BP monitoring (A-line), ventilation support, foley catheter.

• Tachyphylaxis = Decreased response over time.

• When vasopressors is used, the bioavailability of subQ medications can be reduced (due to cutaneous vasoconstriction.)

• Dopamine: more arrhythmias when compare to norepi (24% vs 12%). (SOAP II nejm 2010).

- Increased mortality (meta-analysis).
- Not selectively ↑renal blood flow or prevent renal failure "Renal dose" (ROSE jama 2013).

Recommend reading

• Circulartory shock. N Engl J Med 2013; 369:1726-1734.

• Inotropes and vasopressors: Review of physiology and clinical use in cardiovascular disease. Circulation.2008;118:1047-1056.

• Clinical use of inotropic therapy for heart failure. Circulation.2003;108:492-497.