CARDIOLOGY 2023

VASOACTIVE MEDICATIONS

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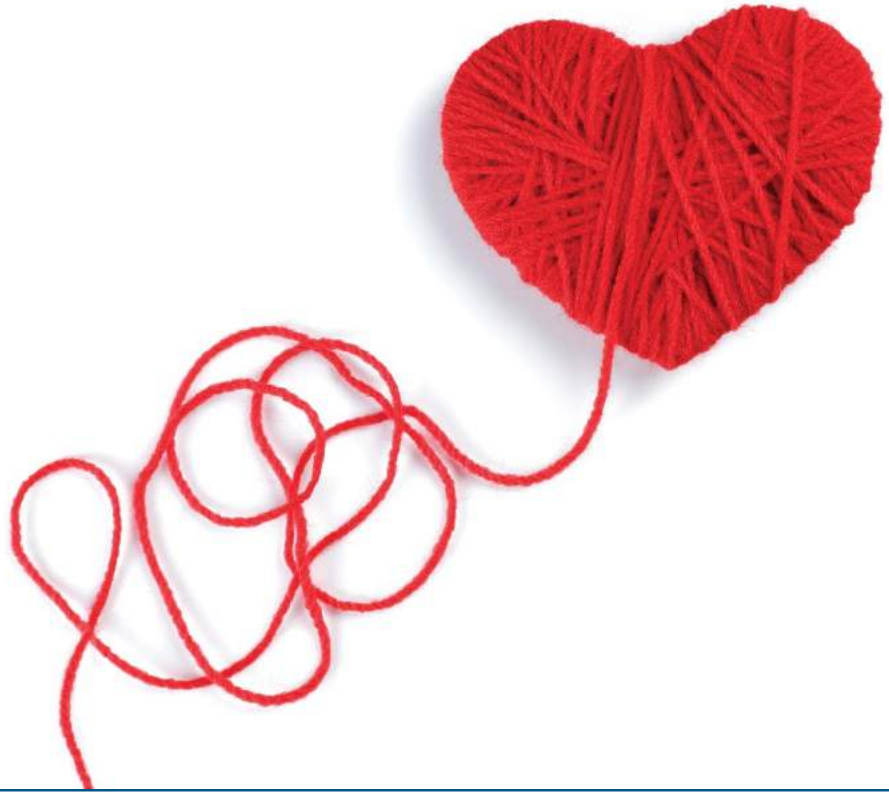


Children's Mercy KANSAS CITY

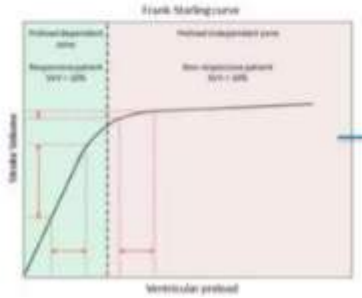
YOU ARE ADMITTING THE NORWOOD

- 5-day-old baby s/p Norwood with 5mm Sanno Shunt
- Milrinone 0.5, Epi 0.06
- Long bypass run
- Tachyarrhythmias in the OR
  - Amiodarone bolus
- TEE shows
  - Mildly decreased function and open shunt
- Hypotensive
- Surgeon reports “all is good”

HEMODYNAMICS

CO = Heart Rate **X** Stroke Volume

- Heart Rate
  - Rate
  - Rhythm
- Stroke Volume
  - Preload
    - CVP
  - Contractility
  - Afterload
    - MAP



Main aim – adequate CO + perfusion to end organs
First correct ↓ CO, then correct ↓ BP

EFFECTS OF BYPASS

- Inflammatory response following CPB
  - Release of systemic and local proinflammatory mediators
  - Activate coagulation/fibrinolytic pathways

- Degree of inflammation associated with:
  - Preoperative conditions (shock, heart failure, etc.)
  - Duration of bypass and cardioplegic arrest
  - Genetic variances

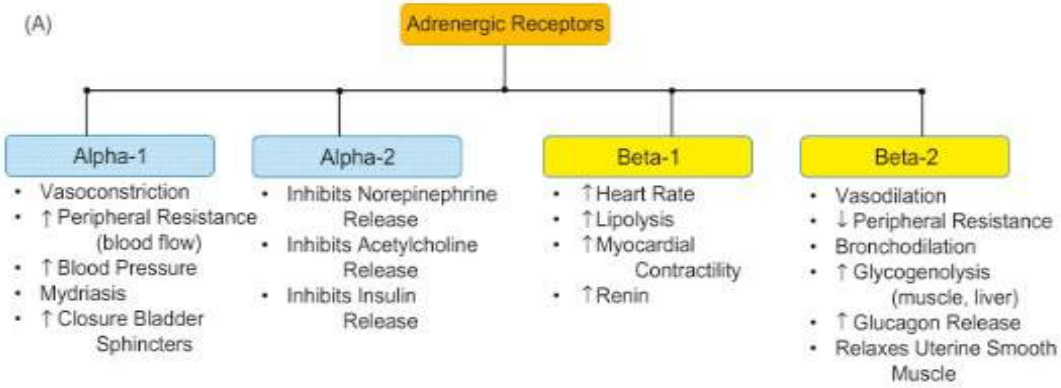
LCOS AFTER CARDIAC SURGERY

- LCOS: Cardiac index < 2.0L/min/m2
- 6-18 hours after cardiopulmonary bypass
- Causes include myocardial ischemia, effects of cardioplegia, residual cardiac lesions
- Organ failure, prolonged hospitalization, inc mortality
- Support myocardial contractility without increasing workload and O2 consumption
- Optimize preload, decrease afterload, decrease O2 consumption

VASOACTIVE MEDICATIONS

- Used to treat hemodynamic instability
- Common cause of morbidity and mortality in critically ill patients
- Choice of vasoactive med will depend on etiology of hemodynamic instability…and may require more than 1 agent
- Blood pressure is important….but so is organ perfusion
  - Altered mental status
  - Decreased CO
  - Decreased renal and hepatic function
  - Cool extremities
  - Shock

ITS ALL ABOUT RECEPTORS



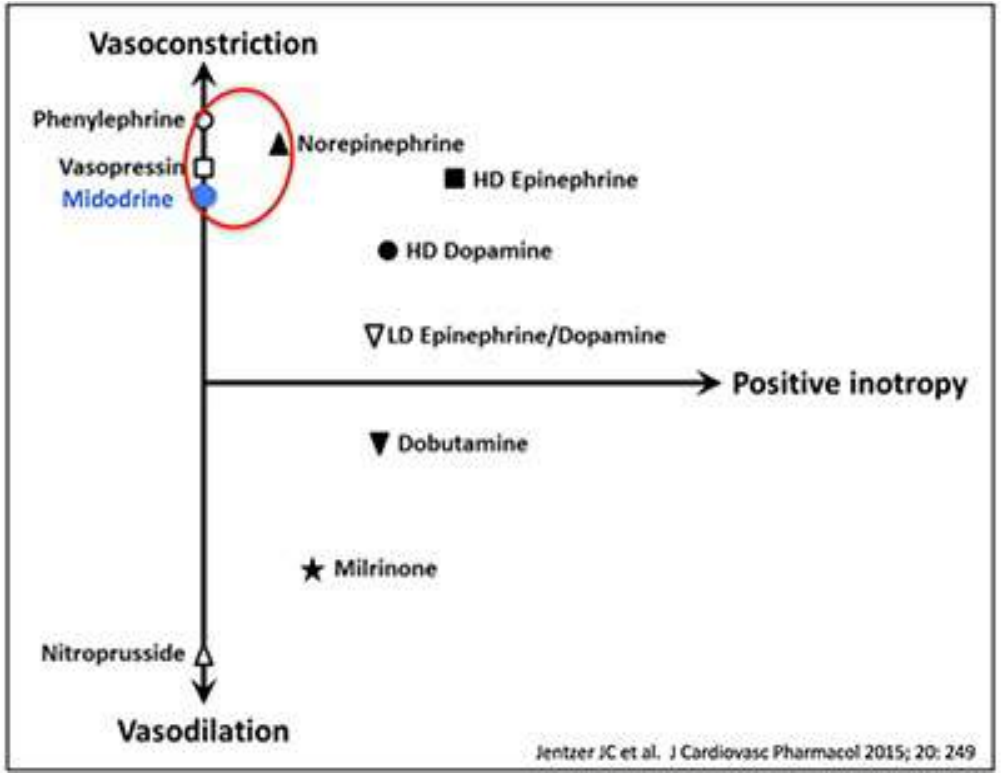
(B)

Alpha-1	Alpha-2	Beta-1	Beta-2
NE > E	E > NE	E = NE	E >> NE
NE = Norepinephrine; E = Epinephrine			

Figure 6.1. Adrenergic receptor subtypes. (A) Physiological effects of catecholamine binding to the specific receptor. (B) Affinity of the receptor subtypes for each catecholamine. ↑=increase, ↓=decrease.

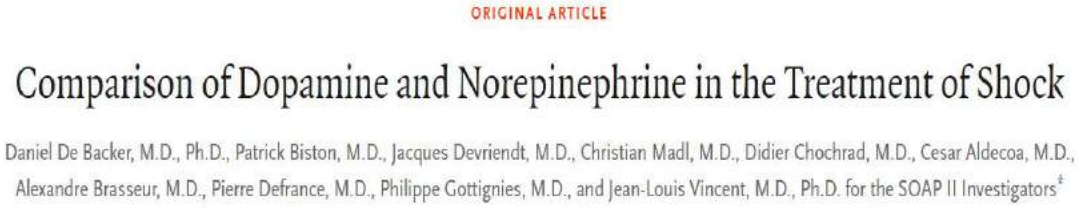
CONSTRICT OR DILATE

- Vasoconstrictors
  - Dopamine
  - Epi
  - Norepi
  - Vasopressin
- Vasodilators
  - Milrinone
  - Nitroprusside
  - Dobutamine



DOPAMINE

- Use: Septic shock, cardiogenic shock, advanced heart failure
- Stimulates both adrenergic and dopaminergic receptors
- Difficult to know what dopamine is doing to your patient
  - Low dose can cause hypotension
  - Increased mortality compared to epi in septic shock
  - Increased myocardial oxygen requirement
  - Greater malperfusion of the gut
  - Can falsely suggest renal perfusion is adequate
- Better agents exist


ORIGINAL ARTICLE

Comparison of Dopamine and Norepinephrine in the Treatment of Shock

Daniel De Backer, M.D., Ph.D., Patrick Biston, M.D., Jacques Devriendt, M.D., Christian Madl, M.D., Didier Chochrad, M.D., Cesar Aldecoa, M.D., Alexandre Brasseur, M.D., Pierre Defrance, M.D., Philippe Gottignies, M.D., and Jean-Louis Vincent, M.D., Ph.D. for the SOAP II Investigators‡

DOPAMINE

- Low dose 1-5mcg/kg/min
  - Increased renal blood flow and UOP
- Intermediate dosing (inotrope) 5-10mcg/kg/min
  - Increased renal blood flow, HR, CO, contractility
- High dose >10mcg/kg/min (vasopressor)
  - Mostly alpha effects with vasoconstriction, increased BP/HR/CO
- Common SE-HA, anxious, N/V, hyperglycemia, anaphylaxis
- Ischemia
  - Myocardial, cutaneous, mesenteric
  - Hyperglycemia and renal vasoconstriction, anaphylaxis
- Can by VERY arrhythmogenic
- Extravasation can be severe

EPINEPHRINE

- Use: Cardiopulmonary resuscitation, anaphylaxis, cardiogenic shock, bronchospasm, low output after bypass, hypotension
- Stimulates alpha, beta 1 and beta 2 receptors
  - Increase HR, contractility
  - Increase SVR high dose (0.2)
- + chronotrophy/inotropy; increase CO
- Increase SVR and vasoconstriction
- 100x more potent inotrope than dopamine or dobutamine

EPINEPHRINE

- Hypotension, poor CO, shock
  - Low dose 0.01-0.1 mcg/kg/min
  - High dose 0.1-0.5 mcg/kg/min
    - Causes vasoconstriction and inotropic effects
    - Can increase myocardial oxygen consumption
- Use caution with beta blockers and tricyclic antidepressants
- Tachycardia
- Hyperglycemia

NOREPINEPHRINE

- 1st line vasopressor for most forms of shock with vasodilatation and severe hypotension
- Not first line choice for cardiogenic shock
- Stimulates beta and alpha adrenergic receptors
  - Increase SVR, venoconstriction (increase preload), + chronotropic effect
  - Increased blood pressure and may increase UOP
  - Can increase CO

NOREPINEPHRINE

- Septic shock
  - Initial 0.05-0.1mcg/kg/min
  - Maximum 2mcg/kg/min
- Post cardiac arrest
  - Initial 0.05-0.1mcg/kg/min
  - Maximum 1-2mcg/kg/min
- Common side effects include anxiety, SOB, dizziness, HA, N/V, diaphoresis, slow HR, urinary retention
- Serious side effects include respiratory distress, numbness of extremities, malignant hypertension
- Vesicant

VASOPRESSIN

- Stimulates V1 and V2 receptors
  - Vasoconstriction and renal water retention
  - Increases SVR
  - Increase preload (venoconstriction)
  - Increased afterload

Effects of Vasopressin Infusion After Pediatric Cardiac Surgery: A Meta-analysis

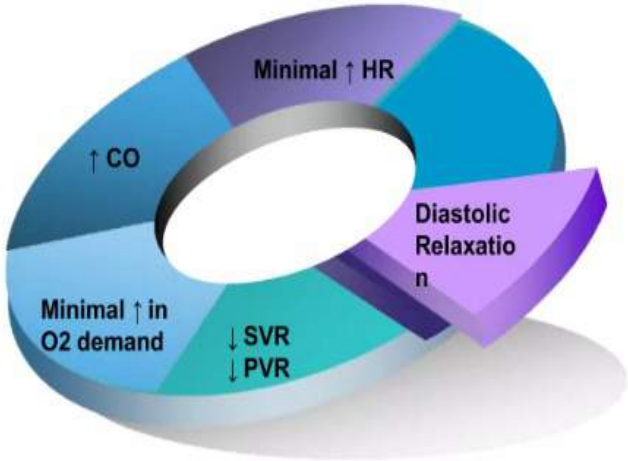
Juan S. Farias[1] · Enrique G. Villarreal[1,9] · Saul Flores[2,3] · Christopher W. Mastropietro[4,5] · Maggie Vogel[6,7] · Kelci Schulz[6,7] · Corissa Culichia[6,7] · Ilias D. Iliopoulos[8] · Ronald A. Bronicki[2,3] · Rohit S. Loomba[6,7]

VASOPRESSIN

- Complex cardiac procedures
- Vasodilatory shock
- Hepatorenal syndrome
- Dose 0.08-1 U/min
- Titrate based on BP
- May increase myocardial oxygen consumption
- SE include arrhythmias, AKI, hyperglycemia, bleeding, hypoperfusion

MILRINONE

- Phosphodiestarase III inhibitor
  - Decrease SVR and afterload
  - Increase contractility
  - Lusitropy
- Used to treat impaired cardiac function, refractory HF, PHTN and RVF, post-op cardiac pts
- Used to help prevent LCOS
- Will not increase myocardial oxygen demand



MILRINONE

- To bolus or not?
  - 50-75mcg/kg over 1 hr
- Continuous infusion
  - 0.25-1mcg/kg/min
- Arrhythmias-SVT, junctional and ventricular tachyarrhythmias
- Hypotension
- Headache

Prevention of Low Cardiac Output Syndrome After Pediatric Cardiac Surgery: A Double-Blind Randomized Clinical Pilot Study Comparing Dobutamine and Milrinone*

Anna Cavigelli-Brunner, MD[1,2]; Maja I. Hug, MD[2,3]; Hitendu Dave, MD[2,4]; Oskar Baenziger, MD[2,3]; Christoph Buerki, MD[2,5]; Dominique Bettex, MD[6]; Vincenzo Cannizzaro, MD, PhD[2,3]; Christian Balmer, MD[1,2]

NITROPRUSSIDE

- Reduces afterload
  - Relaxes Smooth Muscle to:
  - Decrease SVR & Pulmonary Vascular Resistance (PVR)
- Dose Range: 0.3 – 8 mcg/kg/min
- Titrate by 0.5 mcg/kg/min q 15 min
- SE: Hypotension, Cyanide Toxicity w/long term use

DOBUTAMINE

- Directly stimulates beta adrenergic receptors.
  - Inc CO by increasing stroke volume
  - Decreased PVR
  - Increases contractility but also increases myocardial oxygen consumption
- Dosage 2.5 -10mcg/kg/min
- Usage – heart failure, s/p open heart surgery
- Side effects – can be arrhythmogenic, tachycardia, HTN, N/V, chest pain
- Sulphite sensitivity – use cautiously in those with sulfa allergy

YOUR PATIENT

- Mil 0.5 and Epi 0.06
- Hypotensive
  - Have given 3 fluid boluses
- What to do with your vasoactive support?
- Remember pt had tachyarrhythmias in the OR
  - Increase epi?
  - Increase Milrinone?
  - Add another agent?
    - If so which one?

ADD A 2ND AGENT

- Low dose vasopressin vs low dose nor-epi

Rough properties of various vasopressors

Drug Typical dose range	Target	Effect on - Heart rate - Inotropy - Ectopy	Effect on systemic vascular resistance	Effect on cardiac output	Effect on blood pressure	Effect on pulmonary vascular resistance	Main uses	Safe for peripheral use?
Inodilators								
Dobutamine 2-20 mcg/kg/min	αββββ	⇑⇑⇑	⇓	⇑⇑⇑	Variable	⇓	Cardiogenic shock	
Milrinone 0.375-0.75 mcg/kg/min	cAMP	⇑⇑⇑	⇓⇓	⇑⇑⇑	Variable	⇓⇓	Cardiogenic shock	
Isoproterenol 2-10 mcg/min	ββββ	⇑⇑⇑⇑⇑	⇓	⇑⇑⇑	Variable		Bradycardia	Yes
Pure Vasopressors								
Vasopressin 0.01-0.06 U/min	V1 & V2	⇓	⇑⇑⇑	⇔/⇓	⇑⇑⇑	⇓	Distributive shock, Pulmonary HTN	No.
Phenylephrine 40-180 mcg/min	αααα	⇓	⇑⇑⇑	Variable	⇑⇑⇑	⇑⇑	Distributive shock	Yes
InoPressors								
Norepinephrine 0-40 mcg/min*	αααβ	⇑	⇑⇑⇑	⇔/⇑	⇑⇑	⇔	Shock (most types)	Yes, for short period with monitoring
Epinephrine 0-20 mcg/min*	αββββ	⇑⇑⇑	⇑	⇑⇑⇑	⇑⇑		Bradycardia, cardiogenic shock, sepsis, anaphylaxis	Yes
Dopamine, low 1-4 mcg/kg/min	Dopa-R	⇔	⇓	⇑	⇓		Zombie apocalypse (absence of better agents).	Probably not
Dopamine, medium 4-10 mcg/kg/min	αββββD	⇑	Variable	⇑⇑	Variable			
Dopamine, high 10-20 mcg/kg/min	αααβD	⇑⇑	⇑⇑	⇑	⇑⇑⇑	⇑		

*Listed ranges are typically used doses in the United States, but there is no true "maximal" dose. Some countries may tend to use higher doses than others. At very high doses, pressors may lose some receptor specificity. The best dose is the dose required to keep the patient alive – in some cases very high norepinephrine or epinephrine doses may be needed.

-The Internet Book of Critical Care, by @PulmCrit

QUESTIONS?

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