Vasopressors, Inotropes, Shock, Sepsis and the ICU

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Overview

• Definitions
• Approach to diagnosis
• Approach to management
• Experimental treatments and personal bias
• Summary and recommendations
Shock: Definition

The failure of the circulatory system to maintain adequate delivery of oxygen and other nutrients to tissues, leading to cellular and then organ dysfunction.
Diagnostic Approach to Shock

- Refer for ICU help as soon as shock suspected
- Move to ICU at discretion of ICU attending or deputy
- Establish basic monitoring and baseline labs
- H + P, emergent treatment, assess need for advanced monitoring
- Establish advanced monitoring and obtain hemodynamic profile
- Correct hemodynamic disturbance
- Address underlying cause
- Protect end organs
ICU Referral for Assessment of Potentially Shocked Patients

- As early as possible
- Does not automatically imply ICU admission
- ICU attending or deputy will (hopefully) review stat, within 1 hr or within 4 hrs depending on urgency
- Early referral to a comprehensive ICU service improves outcome in shock
Basic Monitoring and Labs

• Monitoring:
  • EKG, SpO$_2$, NIBP, Foley, Fluid I/O

• Labs:
  • CBC, Lytes, Coag, ABG, LFT, Lactate, Cortisol
History and Examination

• Working diagnosis: cause of shock
• Time course of recent decline
• Attempts to correct problem eg diuretic use
• Other medical diagnosis, prognosis and extent of care requested
• Moribund, severely ill or preventive
Emergent Treatment of Shock

• Usually means immediate measures to maintain MAP to keep patient alive
• Often coexists with respiratory support
• Should follow ABC approach to any sick pt
• Only indication for vasopressor use in presence of hypovolemia
Need for Advanced Monitoring

• No hard evidence that use of hemodynamic monitoring improves or worsens outcome, assumption is that it does
• We should have a low threshold for using the hemodynamic monitoring available to us
• Decision left to discretion of attending intensivist
Which Monitor?

- Decide on these criteria:
  - Reliability of data
  - Speed of data acquisition and ease of use
  - Risk of complications
  - Familiarity of nursing staff with equipment
  - Cost
Hemodynamic assessment

• The global cardiovascular picture
• Applied physiology in practice
Basic definitions

• Cardiac output
• Cardiac index
• Heart rate
• Blood pressure
• Filling pressures
• PA pressure
• Shock
Basic physiology

• Cardiac output

Cardiac output

- Heart rate
- Heart rhythm
- Preload
- Contractility
- Afterload
Heart rate and rhythm

- Best 90-110 bpm
- >130 impaired filling
- <60 inefficient
- Sinus rhythm very important
Preload

• Is a volume not a pressure!
Contractility
Afterload

- Left ventricular wall stress
- Arterial vasoconstriction
Afterload

- Best estimate is probably LV wall stress
- Is derivable with echo but v. big equation!
- Most use SVR and SVRI
- SVR = 80 x (MAP - CVP) / CO or CI
- Normal SVR is 900-1300 dyne.sec/cm^5
- PVR and PVRI for pulmonary circulation
- Normal PVR is about 100 dyne.sec/cm^5

Dyne = unit of force
Pressure = force / area = dyne/cm^2
Resistance = pressure / flow
R = (dyne/cm^2) / (cm^3/sec)
SVR = dyne.sec/cm^5
Diagnosing hypotension

• MAP = CO x SVR

• Rate
• Rhythm
• Preload
• Contractility
• Afterload

One or more have changed.
Full Hemodynamic Profile

- For those patients with suitable monitors in place
- Hemodynamic profile eg q 12 hrs
- More often according to severity of illness eg:-
  - q 6 hrs for those on significant doses of vasoactive agents
  - q 1 hr for those who are unstable
  - 30 mins after each major therapeutic change
Correct Hemodynamics

• Administer fluids, inotropes and vasoactive drugs to restore:
  • An effective circulation
  • An effective mean arterial pressure
  • An effective oxygen carrying capacity
• Give fluids and drugs according to need and not just as a routine
• Deviate from guidelines with a clinical reason to do so
Address the Underlying Cause

- Control bleeding eg Surgery, Endoscopy
- Thrombolysis as indicated for acute MI
- Acute anaphylaxis protocol
- Seek cause of pump failure if not ischemic
- Source control, antibiotics and adjuvant therapies for sepsis
Protect End-organs Today to Prevent MODS Next Week

• Renal
• Pulmonary
• Gastro-intestinal
• Lines
• Thromboprophylaxis
Hemodynamic Goals and Resuscitation Endpoints

- Restore effective circulation
- Maintain tissue oxygen delivery
- Maintain tissue nutrient delivery
- Normalize cellular metabolism
Specific Endpoints

- Blood Pressure: MAP is the main determinant of perfusion in a pulsatile circuit: at least 60 and sometimes 90
- Lactate: High levels correlate with poor outcome. Low levels do not rule out underperfusion
- $SvO_2$: Useful if low. Normal value does not rule out underperfusion
Clinical Indices of Adequate Perfusion

- Good urine output (1ml/kg/hr)
- No angina
- No reduction in conscious level
- Good capillary return
- Warm extremities
Base Excess (Deficit)

• Provides estimate of metabolic component of acid-base upset
• Correlates well with extent of metabolic upset and trend indicative of overall “wellness”
• Extremely useful (and widely underused) indicator of adequacy of resuscitation
Shock Therapy

- Fluids
- Inotropes
- Vasoactive drugs
- Experimental treatments
Aims of Fluid Therapy

• Convert hypodynamic situation to normal or hyperdynamic state
• Increase cardiac output until either effective circulation restored or plateau reached on Starling curve
• Blood: Always if Hb < 7 g/dl
  Never if Hb > 10 g/dl
  For symptoms if 7-10
Aims of Inotropic Therapy

- Restore an effective cardiac output when optimum fluid therapy alone has not
- Primary effect is to increase CO not MAP
- No justification for routine elevation of CI to 4.5 l/min/m²
- Evidence of tissue underperfusion with CI less than 3.0 after optimum fluid replacement would suggest an inotrope
- Add vasopressor when CI > 4.0 and MAP still low
Aims of Vasoactive Therapy

- Restore MAP when optimum fluid therapy and appropriate inotropic therapy have not
- Vasopressor treatment may be needed emergently while fluid therapy is underway
- All who receive vasoactive therapy in the ICU should have an A-line in place
- A-lines: Radial – Femoral – Axillary
Fluids in Shock

- 50% of patients with hypotension will respond to fluid therapy alone
- Type not as important as how and how much
- Give by bolus and against an index of preload
- Encourage bedside generation of dynamic Starling curve
Starling Curve

![Starling Curve Graph](chart.png)
Fluid Type

- N/saline and LR are both roughly iso-osmolar.
- About 20% remains intravascular
- Less hyperchloremic acidosis with LR
- 5% albumin replaces volume 1:1
- 25% albumin replaces 5:1
- Hespan replaces 1:1 but prolongs PTT and reduces FVIII activity
Fluid Type Facts

- Need less colloid to achieve same hemodynamic endpoints
- Colloids are more expensive
- Colloids produce less tissue and pulmonary edema, even in ARDS
- Recent meta-analyses exist to show that albumin is harmful (Cochrane) and that it is not (Choi)
- SAFE trial showed us that colloid and crystalloid equally effective
Dynamic fluid therapy

• Give a fluid bolus e.g. 200 ml crystalloid
• See what happens
• CVP stays the same = empty
• CVP goes up ++ = full
• Normal = CVP goes up and comes down again
• Elevate the legs if not sure
Inotropes

- Options:
  - Epinephrine
  - Dobutamine
  - Dopamine
  - Milrinone
  - (Glucagon)
Dobutamine

- $\beta_1$ and $\beta_2$ effects from $\delta$-isomer
- $\beta_1$ and $\alpha_1$ effects from $\lambda$-isomer
- Overall $\beta_1$ effects predominate leading to raised CI and some dilatation: “Inodilator”
- May also increase HR
- $\beta_1$ agonists are also anti-inflammatory in clinical doses
Epinephrine

• Raises cardiac index
• Raises heart rate
• Raises MAP
• Raises VO$_2$
• Reduces gut perfusion
• Generates lactate
Dopamine

• Raises HR
• Raises CI
• Raises MAP
• Raises VO$_2$
• Reduces gut perfusion
• Is immunosuppressant (reduces prolactin and T cell function)
• May worsen outcome in shock
Milrinone

- Raises CI
- Reduces MAP
- Proarrhythmic
- Long $t_{1/2}$
- Good pulmonary vasodilator
- Often needs a pressor for optimum effect
Vasopressors

• Use *after* fluids and inotropes have failed to restore MAP

• Options:
  • Dopamine
  • Norepinephrine
  • Epinephrine
  • Phenylephrine
  • Vasopressin
Dopamine

- Different response at different doses
- Different response in different patients
- Does increase urine output
- Does not increase waste clearance
- Wide dose range allows maintenance of MAP while ignoring extreme hypovolemia (ie hides physician inattention)
Norepinephrine

- Predominant $\alpha_1$ effects
- Some $\beta_1$ effects, which protect gut
- 70’s dog studies frightened people away
- Increases RBF if volume replete
- Will work when dopamine will not
- Good in conjunction with dobutamine and / or milrinone
Epinephrine

- Mainly $\alpha_1$ and $\beta_1$ effects
- Causes much more tachycardia than others
- Increases MAP by increasing CI mainly
- Increases $\text{DO}_2$ but at cost of $\text{VO}_2$ especially cardiac
- Reduces gut and renal blood flow
- Increases lactate levels
**Phenylephrine**

- Very potent $\alpha_1$ agonist
- No $\beta$-mediated gut or renal protection
- Some intrinsic vasopressor activity outside realm of $\alpha_1$ receptor (cf hydralazine)
- Sometimes works when Norepi doesn’t
Vasopressin

- Septic patients are deficient
- 0.04-0.1 u/min may completely replace other pressors
- Question over peripheries, gut and renal circulation in high dose
- Add in when other doses begin to rise, not just before train leaves.
Vasopressor Recommendations

1. Norepinephrine
2. Vasopressin
3. Phenylephrine
4. Epinephrine
Conclusions

• Think about the physiology
• Use all the information available
• Consider flow before pressure
• Remember the importance of $\text{SaO}_2$ and Hb
• Tissues also need a perfusion pressure
Summary

• Encourage early referral
• Be aggressive with monitoring and look for hemodynamic trouble
• Use more colloid
• Use no dopamine
• Use drugs according to clinical situation eg epi great for sick heart, norepi better in sepsis
Questions?

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