VASOPRESSORS AND INOTROPES

CLINICAL PROFESSOR ANDREW BEZZINA FACEM

MAY 2017
CONFLICTS OF INTEREST
OVERVIEW

- Why?
- When?
- What?
- How?
WHY?

Circulation
WHY? - SHOCK!!!

- **HYPOVOLEMIC** – the pipes have a hole in them (haemorrhagic) or they are leaky (non haemorrhagic)
- **SEPTIC** – the pipes are leaking and the pump is failing
- **ANAPHYLACTIC** – the pipes are leaking and the pump is failing.
- **CARDIOGENIC** – the pump is failing. Can’t squeeze **hard enough** OR can’t squeeze **fast enough**
THE CONTINUUM OF SHOCK

NORMAL STATUS

COMPENSATED SHOCK

DECOMPENSATED SHOCK

IRREVERSIBLE SHOCK

DEATH

ZONE OF OPPORTUNITY
STARTING

Prerequisites and Precautions

• Tank must be full
• No contraindications
• Appropriate access
WHAT LEVERS?

• **Alpha-1 adrenergic receptors:**
  • Induce significant vasoconstriction.
  • Can increase the duration of contraction without incr PR

• **Beta adrenergic receptors:**
  • Beta-1: increase in inotropy and chronotropy with minimal Vc
  • Beta-2: induces vasodilation in skeletal muscle.

• **Dopamine receptors:**
  • In the renal, splanchnic (mesenteric), coronary, and cerebral vascular beds. Induces vasodilation.

**LEVERS**

- **Vasopressin Receptors** – Vasopressin/ Terlipressin

- **Altering Intracellular activity** –
  - Levosimendan – modulates Troponin
  - Milrinone – cAMP phosphodiesterase 3 inhibitor.
WHAT TOOLS?

• **Inotropes** - increase myocardial contractility (inotropy)
  — e.g. adrenaline, dobutamine, isoprenaline, ephedrine

• **Vasopressors** - cause vasoconstriction leading to increased systemic and/or pulmonary vascular resistance (SVR, PVR)
  — e.g. noradrenaline, vasopressin, metaraminol, methylene blue

• **Chronotropes** – increase rate e.g. isoprenaline, dobutamine

• **Atypical** - don’t fit categories easily e.g. dopamine
Pump Harder
WHICH TOOL?

So many tools... so little time...
THE REAL QUESTION

WHATTTTTTT

ARE YOU TRYING TO DO
SHOCK IN GENERAL

• In most common situations of circulatory shock (sepsis, toxins) trying to increase both vasoconstriction and cardiac contractility (squeeze the vessels AND pump harder)

• What does the evidence say?
PROBLEMS WITH THE EVIDENCE

• First and foremost - there are **no definitive RCTs** to prove that vasopressors/inotropes provide better outcomes than placebo.

• **There are also no RCTs comparing jumping out of a plane with a parachute is safer than jumping without.**

• There is some evidence BUT most are small number **comparisons of one agent vs another** and often in different types of shock).
Evidence is insufficient to prove that any of the vasopressors at assessed doses are superior over others in terms of mortality.

Dopamine increases the risk for arrhythmia and might confer a mortality disadvantage versus noradrenaline.

The choice of the specific vasopressor may therefore be individualized and left to the discretion of the treating physician.
Factors should be considered such as

- **Experience** (what are you used to using?)
- **Physiological effects** (e.g. heart rate, intrinsic inotropic effects, splanchnic perfusion)
- **Drug interaction** (e.g. vasopressin and concomitant use of corticosteroids) (Russell 2009),
- **Availability and cost**
CONSIDER

• 48 year old male presents unwell, confused and hypotensive with no history of trauma or blood loss.

• Airway normal, RR 24, Chest clear, O2 Sat - poor trace ?90%,

• PR – 138, BP 66/40, CR 4 seconds and cool peripheries.

• Volume – 30ml/kg given

• PR 132, BP 72/46, Cool peripheries.
NUTSHELL

• Shocked patient, cause unclear no response to volume, no infusion pump available!

• No Method of close monitoring possible?

Initial Solution – THE DIRTY ADRENALINE INFUSION
1mg in 1 litre (1microgm/ml) 5% Dextrose or Normal Saline and start running slowly. Adjust rate as necessary every 5 minutes after checking PR and BP response.

Option 2 - Method of close monitoring of infusion possible
e.g. Reliable Drip count / Syringe pump –

Local infusion protocol for concentration/rate
SPECIFIC SETTINGS - ANAPHYLAXIS

• In this setting the problem is complex with vasodilation and capillary leakage as well as poor pump function.

• AIM – vasoconstriction (squeeze) and inotropy (pump harder).

• The agent of choice and only one for which there is any evidence base is –

ADRENALINE
SPECIFIC SETTINGS - SEPSIS

• Like anaphylaxis it’s complex with vasodilation and capillary leakage as well as poor pump function.

• AIM – vasoconstriction (squeeze) and inotropy (pump harder).

• The most commonly used agent is Noradrenaline.

NORADRENALINE
Compared to Dopamine, Noradrenaline is associated with decreased all cause mortality, RR 0.89 (95% CI 0.81-0.98), absolute risk reduction of 11%, NNT= 9.

Scandinavian Guidelines

1. We recommend that norepinephrine is used as first-line vasopressor for patients with septic shock rather than dopamine (strong recommendation, moderate quality of evidence).

2. We suggest that norepinephrine is used as first-line vasopressor for patients with septic shock rather than epinephrine (weak recommendation, low quality of evidence).
SPECIFICS – CARDIOGENIC SHOCK

• Question 1 –

What’s the problem - Rate or Contractility or both?

Determines the aim – Pump harder or pump faster (or both).
CONSIDER

• 67 year old male RVD positive – unwell and SOB

• RR 28, Oxygen saturations 88%, Crackles to midzones and CXR pulmonary oedema.

• Pulse rate 36

• BP 180/70

• ECG complete heart block (potassium normal)

• Which agent?
TREATMENT

• Problem = Rate

• Aim – increased rate = chronotrope.

• Pharmacological Options –
  a) Isoprenaline/ Dobutamine
  b) Adrenaline infusion if above not there.
CONSIDER – SAME CASE

• BP 80/56 – consistent with cardiogenic shock

• Problem – Rate AND BP

• Aim – increase pulse rate AND increase contractility.

• Options –

a) Isoprenaline/Dobutamine may still work alone.

b) Noradrenaline alone or in addition

c) Adrenaline – no data available.
SAME CASE

• PR 112, BP 88/54

• Problem – BP (hypoperfusion)

• Aim – increase contractility +/- vasoconstriction

• Options –
  a) Noradrenaline
  b) Dopamine – evidence of increased risk of arrhythmias
  c) Adrenaline – no data available.
**HOW?**

- All sympathomimetic agents are diluted in saline 0.9% or in 5% dextrose.

- **Infusion protocols vary from facility to facility.**

- Key is to have a set protocol that all clinicians and all departments in the same hospital use so that error is minimised.

- **It is **NOT** necessary** to have a central line for the commencement of these agents - even vasopressors.

- **Don’t “set and forget“** – always monitor response and adjust

STOPPING
QUESTIONS

KEEP CALM AND PUMP IT
KEY POINTS

• Vasopressors won’t work if the tank is empty \textit{(adequate volume first)}

• Consider what you are trying to achieve – Pump harder OR Squeeze tighter?

• In a jam with limited resource? \textit{Use what you have} (The dirty adrenaline infusion is a great temporising option).

• Limited evidence would suggest Noradrenaline is the agent of choice in sepsis, toxic shock, profound cardiogenic shock or shock of unknown cause.

• Vasopressors/Inotropes do not mandate Central Access
That's all Folks!