Cardiovascular Resuscitation
Restoring function & Preventing harm

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ARC Guideline 13.9
- Continuing care of the newborn infant after resuscitation (Cardiorespiratory)
  - Oxygen saturation
  - Heart rate
  - Respiratory rate
  - BSL/ABG
  - Blood pressure

Case
- Uncomplicated pregnancy
- Normal vaginal delivery
- 38 weeks, BW 3500gm
- Apgar score 9/9
- Post natal hypoxic episode age 1hr requiring full CPR
- Severe hypoxia/acidosis
- Transfer to tertiary centre on ventilator

Case
- Monitoring in NICU
  - Respiratory
  - Neurological (aEEG)
  - Metabolic
  - Cardiovascular (BP)

BP chart
- Sys BP 46-55 mmHg
- MBP 32-43 mmHg
Case
CPU/fECHO at age 16 hrs

- Very low Doppler velocity in RV outflow tract
- 0.35m/sec – normally >0.5m/sec

Calculated RV output was 65ml/kg/min
Normally >150mls/kg/minute

Treatment options
- Do nothing – BP is within normal range
- Treat low cardiac output/myocardial dysfunction
  - Volume
  - Inotrope/Vasopressor options
    - Dopamine
    - Dobutamine
    - Adrenaline
    - Milrinone
    - Vasopressin

Case
CPU/fECHO at age 16 hrs

Poor contractility visually, particularly of LV
Treatment options

- Do nothing – BP is within normal range
- Treat low cardiac output/myocardial dysfunction
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    - Dopamine
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Case
CPU/fECHO 24 hrs later on Rx

- Improved contractility
- RVO now 180ml/kg/min

Cardiac output ≠ Blood Pressure
Role of SVR

- Other studies have also found a poor relationship between blood pressure and blood flow
- Wardle et al. Ped Research 1999; 45(3): 343-9

HIE/Asphyxia signs are similar to shock

- Pale
- Poor skin perfusion
- Hypothermia
- Poor cardiac output
- Reduced vital organ perfusion
- Lactic acidosis
- Tachycardic
- Early compensation
Neonatal Shock
Overlaps with asphyxia
- Inadequate oxygen delivery to the tissues to satisfy demand

Phases of neonatal shock
- Compensated (Early)
  - Neuroendocrine compensation maintains vital organ blood flow
  - Normal systemic BP but changes in HR, CRT and urine output**
- Uncompensated
  - Failure of neuroendocrine compensation
  - Hypotension**, decreased vital organ perfusion and lactic acidosis
- Irreversible
  - Irreparable damage to tissues
  ** Identification/definition in preterm infant may be difficult

Cardiovascular dysfunction in the post asphyxial period
- Hypovolaemia (capillary leak, venodilation)
- Hypoxia induced cardiac dysfunction
  - Reduced myocardial contractility (asphyxia, acidosis)
  - Passive dilatation
- Decreased systemic blood flow from reduced pulmonary venous return
  - Increased PVR
- High ventilation requirements
- Systemic hypotension (decompensation)
- Impaired cerebral auto-regulation (post LCOS)
- Impaired peripheral vasoregulation/Distributive failure
- Cellular failure – inability to utilize oxygen

Definer 2003; Crit Care Med, Joynt & Cheung Current Pediatric Reviews 2009
Cardiac index in asphyxia

- Newborn piglet model
- Hypoxia followed by resuscitation with RA or 100% oxygen
- 50-60% increase initially, rapid decline to half of baseline, then recovery but less than baseline
- BP maintained better than CI


Myocardial damage
Biochemical/Echo/ECG

<table>
<thead>
<tr>
<th></th>
<th>Asphyxiated</th>
<th>Control</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trip (%)</td>
<td>0.15 (0.10-0.23)</td>
<td>0.05 (0.02-0.15)</td>
<td>0.007</td>
</tr>
<tr>
<td>Echo EF (%)</td>
<td>22 (19%)</td>
<td>22 (19%)</td>
<td>0.98</td>
</tr>
<tr>
<td>LVd (mm)</td>
<td>41.6 (6.8)</td>
<td>41.5 (6.8)</td>
<td>0.98</td>
</tr>
<tr>
<td>LVs (mm)</td>
<td>14.6 (2.7)</td>
<td>15.3 (2.0)</td>
<td>0.33</td>
</tr>
<tr>
<td>LVd (ml/min/kg)</td>
<td>88.2 (18.3)</td>
<td>75.2 (17.2)</td>
<td>0.025</td>
</tr>
<tr>
<td>SV (ml/kg)</td>
<td>2.7 (1.2)</td>
<td>4.6 (1.2)</td>
<td>0.005</td>
</tr>
<tr>
<td>ESWS (g/cm2)</td>
<td>34 (23.9-51.3)</td>
<td>30 (20.6-52.1)</td>
<td>0.39</td>
</tr>
<tr>
<td>Preh ECG score</td>
<td>0.8 (0.3-1)</td>
<td>0.9 (0.3-3)</td>
<td>0.34</td>
</tr>
<tr>
<td>ECG grade</td>
<td>3</td>
<td>0</td>
<td>0.005</td>
</tr>
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Enzymatic and instrumental data from asphyxiated and control infants.

Cardiac dysfunction is a common complication of a hypoxic-ischaemic insult (varies from 50-80% in series)

- Significant cardiac dysfunction may further impair component of adequate tissue oxygenation
- Not identified by ECG changes or BP monitoring
- Cerebral perfusion is directly related to cardiac output so will decrease with cardiac dysfunction
- This may be exacerbated by impaired cerebral auto regulation (more common with asphyxiation)
- Significant cardiac dysfunction may further impair neurological outcome in HIE

Asphyxia & LV Dysfunction

- 40 Term infants with HIE – acidosis, neurological dysfunction, multi-organ dysfunction. 28 LVDF, 12 No LVDF
- 30 healthy controls
- MCA cerebral Dopplers
- Evidence of LV dysfunction(EF/reduced cardiac output) in HIE group
- 15/28 with LVDF developed a severe encephalopathy
- 1/12 without LVDF developed severe encephalopathy

Asphyxia - Summary

- Maintenance of cardiac output is an important component of adequate tissue oxygenation
- Cardiac dysfunction is a common complication of a hypoxic-ischaemic insult (varies from 50-80% in series)
- Not identified by ECG changes or BP monitoring
- Cerebral perfusion is directly related to cardiac output so will decrease with cardiac dysfunction
- This may be exacerbated by impaired cerebral auto regulation (more common with asphyxiation)
- Significant cardiac dysfunction may further impair neurological outcome in HIE


Liu 2007; J Tropical Pediatrics
Can we pick “poor perfusion” clinically?

- Superior vena cava flow - proxy for cerebral blood flow
- Use of low SVC flow as a gold standard
- 45 VLBW infants – SVC flow measured and compared to:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Correlation Coefficient</th>
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<tbody>
<tr>
<td>Capillary refill time</td>
<td>r = .008, r = 0.1</td>
</tr>
<tr>
<td>Urine output</td>
<td>r = .189</td>
</tr>
<tr>
<td>Mean BP</td>
<td>r = .248</td>
</tr>
<tr>
<td>Serum lactate</td>
<td>r = .28</td>
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Miletin J. Eur J Paediatrics 2008 EPub

Assessment of perfusion

Clinician Performed Ultrasound (CPU)

- Bedside
- Real time
- Serial
- Focused
- Target treatment
- Monitor response
- Refine clinical decisions
- Understand physiology
- Function mainly

CPU - Uses in asphyxiated neonate

- Assess volume status
  - Vein distension/compressibility
- Assess chamber size (esp. end diastolic)
  - Atria
  - Ventricles
- Assess contractility
- Diastolic function - MPI
- Measure cardiac output - RVO, LVO
- Ventricular interdependence/septal bowing
- Assess pulmonary pressures (TI/Ductal shunt)
<table>
<thead>
<tr>
<th><strong>Cardiovascular Resuscitation Questions</strong></th>
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<tr>
<td>- In neonates requiring resuscitation does volume administration improve outcome?</td>
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<tr>
<td>- What type of volume – crystalloid vs colloid?</td>
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<tr>
<td>- Inotrope/Vasopressor – need and choice?</td>
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<td>- Bicarbonate?</td>
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<th><strong>Volume</strong></th>
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<td>- No question re value in haemorrhagic or hypovolaemic shock due to perinatal complication</td>
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<tr>
<td>- Neonates unresponsive to chest compressions and adrenaline often receive volume</td>
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<tr>
<td>- Routine post resus use in asphyxiated infants may not be helpful (57% received volume in Wyckoff study)</td>
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Wyckoff, Perlman, Laptook Pediatrics 2005

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<th><strong>Type of Volume</strong></th>
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<td>- Studies generally supportive of crystalloids over colloids as the resuscitative fluid of choice</td>
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<tr>
<td>- As efficacious</td>
</tr>
<tr>
<td>- Less fluid retention</td>
</tr>
<tr>
<td>- Delayed cord clamping – the first step in resuscitation?</td>
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<tr>
<td>- Eg 1 minute delay = 80mls of placental blood</td>
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Raju & Singhal 2012 Clinics in Perinatology
Inotropes/Vasopressors

- Diagnose the underlying disorder
  - Hypotension vs impaired cardiac output
  - Myocardial impairment/failing ventricle vs peripheral vascular resistance anomaly
- Consider the cardiovascular effects of each potential treatment
- Target treatment to the physiology


Inotropes - which to use

- Reciprocal relationship between combined vascular resistance and cardiac output in both healthy and sick neonates
- Eg. Dopamine (vasoconstrictor) may increase BP but may decrease CO, worsen intestinal perfusion and aggravate pulmonary HT

Istvan Seri, 2008

Inotropes/Vasopressors

- Dopamine
- Dobutamine
- Adrenaline
- Milrinone
- Vasopressin
- Hydrocortisone (No term baby studies)

Clinical Trials of Dopamine in asphyxiated neonates

- 14 severely asphyxiated neonates randomised to low dose DA (2.5 mcg/kg/min) or placebo (DBRCT). No difference in outcomes.

Trials of Dobutamine in asphyxiated neonates

- Dose response trial of DB vs placebo during reoxygenation after hypoxia in 38 2 day old newborn piglets. DB at 20 mcg/kg/min improved CI, with modest improvements at 5 & 10.
- Improved systemic oxygen delivery, PVR lower.
- No effect on HR or SAP or regional perfusion.

Clinical Trials of DA/DB in neonates

- No RCT of dobutamine vs placebo.
- 5 RCT’s of dobutamine vs dopamine for treatment of hypotension (Cochrane review, 2003) 143 infants – mostly preterm.
- One additional RCT evaluating dobutamine vs dopamine for low systemic blood flow.
- DA improves BP better than cardiac output.
- DB more useful if myocardial impairment/Low CO.

Adrenaline

- Few trials, but used frequently in the treatment of hypotension in the preterm infant.
- Adrenaline (0.125-0.5 mcg/kg/min) as effective as dopamine at increasing BP and cerebral blood flow (measured by NIRS).
- Both result in increases in myocardial contractility and heart rate.
- Additive to effect of DA and DB, with no apparent adverse excess vasoconstriction effect.
Adrenaline in CVS Resuscitation

Inodilators - milrinone and amrinone
- Selective phosphodiesterase inhibitors
- Increase intracellular cyclic AMP
- Effects on calcium influx, efflux and myofilament calcium binding
Myocardium ⇒ positively inotropic
Vascular endothelium ⇒ vasodilator

Trials of Milrinone in asphyxiated neonates
- Dose response trial of Milrinone vs placebo during reoxygenation after hypoxia in 28 1-3 day old newborn piglets
  - M at low(25 mcg/kg LD,0.25mcg/kg/min), medium(50/0.5) or high(75/0.75)improved CO, Carotid flow and systemic oxygen delivery
  - No effect on HR, SAP or PVR

Vasopressin
- Primarily involved in regulation of osmolarity and fluid homeostasis
- Receptors for vasopressin found in all vascular beds
- Hypotension and vasodilation reduced by vasopressin
- No increase in myocardial oxygen demand
- May be a role for use of VP in shock/resuscitation
- Role in adults post resuscitation established – neonatal use under investigation (P McNamara)
**Bicarbonate**

- Role in resuscitation/post resuscitation unclear
  - Exacerbates intracellular hypercarbia in absence of ventilation
  - May impair myocardial function
  - Neonates rely on anaerobic metabolism for energy source
  - No demonstrated benefit on survival or outcome (prems mainly)

**Conclusions**

- Asphyxia/HIE is commonly associated with cardiac dysfunction
- Maintenance of cardiac output is vital in asphyxia, especially if auto regulation impaired
- Blood pressure does not always identify low cardiac output syndrome
- Enhanced haemodynamic monitoring (CPU)
  - adds extra physiological information
  - helps guide treatment choices
  - documents response longitudinally

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**Conclusions**

- Earlier intervention may be possible
- Need for volume/inotrope choice can be titrated according to physiology
- Possibly better outcomes by maintaining physiological normality
- Cardiovascular dysfunction post asphyxia is generally self limited (Is harm done while we await resolution?)

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