Neonatal Hypotension

Definitions
A uniform definition for neonatal hypotension, especially at the extremes of prematurity, is lacking. In very low birth weight (VLBW) infants in the first few days of life, a mean arterial blood pressure has been proposed to be at or above the gestational age of the infant (in weeks); lower values are considered as hypotension. There is indirect evidence to suggest that auto-regulation may set in (and thus pressure is maintained) at mean blood-pressures above 30mm Hg pressure, with values below being pressure passive. In term infants, it is appropriate to maintain much higher mean blood pressures than their gestational ages, especially if there is persistent pulmonary hypertension.

<table>
<thead>
<tr>
<th>Gestational age</th>
<th>Lower 95% CI for MAP (mm Hg) vs gestational age (weeks)</th>
</tr>
</thead>
<tbody>
<tr>
<td>23</td>
<td>24 25 26 27 28 29 30 31 32 33 34 35</td>
</tr>
<tr>
<td>0–12 hours</td>
<td>20 21 22 23 25 26 27 28 29 30</td>
</tr>
<tr>
<td>13–24 hours</td>
<td>20 22 23 25 27 28 29 30 32 33</td>
</tr>
</tbody>
</table>

Methods of blood pressure measurement also vary, with the two most common being oscillometric (non-invasive cuff blood-pressure on limbs) or invasive arterial (peripheral or umbilical arterial). There is good correlation between non-invasive and invasive pressures when they are in the normal range but oscillometry can over-estimate mean blood pressures when in the hypotensive range.

Physiology
Principal factors governing circulatory function
1) Preload
2) Inotropy
3) Afterload

Frank–Starling curve showing effect of increased inotropy versus increased afterload on stroke volume.

Correlations with outcome
The ultimate aim of maintaining adequate blood-pressure is to ensure satisfactory tissue perfusion. This has proved difficult to measure. Some small studies have suggested white matter damage and poor neuro-development outcome associated with recorded hypotension (variably defined), however, no such correlation was observed in a large cohort of VLBW infants.

Adrenergic and dopaminergic receptor-dependent cardiovascular actions of the most frequently used sympathomimetic agents

<table>
<thead>
<tr>
<th>Agent</th>
<th>Cardiovascular adrenergic and dopaminergic receptors*</th>
<th>Peripheral vascular receptors</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>$\alpha_1$, $\beta_1$, $\beta_2$, Dopamine</td>
<td>$\alpha_2$, $\beta_2$, Dopamine</td>
</tr>
<tr>
<td>$\uparrow$contractility</td>
<td>$\uparrow$conduction</td>
<td>$\uparrow$contractility</td>
</tr>
<tr>
<td>$\uparrow$rate $\uparrow$contractility</td>
<td>$\uparrow$contractility</td>
<td>$\uparrow$Peripheral vaso-constriction</td>
</tr>
<tr>
<td>$\uparrow$Peripheral vaso-constriction</td>
<td>$\uparrow$Peripheral vaso-dilation</td>
<td></td>
</tr>
<tr>
<td>$\uparrow$vasodilation in renal, mesenteric, and coronary circulation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dopamine</td>
<td>++++</td>
<td>+</td>
</tr>
<tr>
<td>Epinephrine</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Norepinephrine</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>Dobutamine</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

*Estimated relative contribution of adrenergic and dopaminergic receptor stimulation to the cardiovascular actions of sympathomimetic amines.
0: no effect; +: minimum effect; ++: maximum effect; $\uparrow$: receptors other than the adrenergic and dopaminergic receptors also mediate some of the cardiovascular actions of the sympathomimetic agents (for example, the dopamine-induced stimulation of the myocardial receptors contributes to the peripheral vaso-constriction caused by higher doses of the drug). $\uparrow$: dopamine stimulates the $\alpha_2$-adrenergic and dopaminergic receptors in a dose-dependent manner; $\uparrow$: only approximately 50% of the positive inotropic effect of dopamine result from the direct stimulation of the myocardial adrenergic receptors ($\uparrow$); the relative contribution of the $\alpha_1$ and $\beta_2$ adrenergic receptors and the myocardial dopaminergic receptors to the increase in myocardial contractility in the neonate is unknown. $\uparrow$: 6-methyldopaebaline, the major dopamine metabolite is a relatively potent and highly selective $\alpha_2$-adrenoceptor antagonist (386). The $\alpha_2$-adrenoceptor inhibitory effects of this metabolite may contribute to the tendency of dobutamine to cause peripheral vasoconstriction. See text for details.
**Cochrane reviews**

- Dopamine was more successful than albumin at correcting low BP in hypotensive preterm infants (Osborn and Evans 2001).
- Dopamine is more effective than dobutamine in the short term treatment of systemic hypotenison in preterm infants (Subhedar and Shaw 2003).
- There are insufficient data on the use of adrenaline infusions in preterm infants with cardiovascular compromise (Paradisis and Osborn 2004).
- Hydrocortisone may be as effective as dopamine when used as a primary treatment for hypotension (Ibrahim, Sinha, and Subhedar 2011)

**Assessment and Management**

A careful clinical and biochemical assessment of a potentially hypotensive infant is an essential first step towards management. This should include: heart rate, capillary refill time, urine output, serum lactate concentration, pH, base excess and haemoglobin. A conservative approach (permissive hypotension) is acceptable if the clinical examination is satisfactory in the face of apparent hypotension.

20mls/kg fluid bolus (0.9% saline over 30-60min). Consideration should be given for the need for blood products (including FFP if clotting deranged).
Assess need for second bolus if remains clinically hypovolaemic.
This may be justified as infants rarely reach the peak of the Frank-Starling curve.

Registrar review before commencing dopamine at 6-10 mcg/kg/min (dose range 2-20 mcg/kg/min). If no response, discuss with consultant. Consider asking for cardiology review and Echo, to help assess filling and ventricular function.

Consider Dobutamine after D/W consultant. Start at 6-10mcg/kg/min (dose range 2-20 mcg/kg/min).
Dobutamine may be inappropriate in profound vasodilatation.

Consider starting Hydrocortisone (2.5mg/kg/dose 6hrly).
Recent evidence shows that a smaller dose of 2mg/kg/day may also be equally effective – discuss dose with consultant.

Consider Adrenaline 0.05-1mcg/kg/min

Consult with cardiology for review and echo if not already involved.

**References**

Ibrahim and Subhedar. 2011. ‘Corticosteroids for Treating Hypotension in Preterm Infants’. Cochrane Reviews
Subhedar, Shaw. 2003. ‘Dopamine Versus Dobutamine for Hypotensive Preterm Infants’. Cochrane Reviews

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