Clinical Guideline: Management of Hypotension in the Neonate

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For use in: Eastern Neonatal Units
Guidance specific to the care of neonatal patients

Used by: Medical Staff

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<table>
<thead>
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<tbody>
<tr>
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</tbody>
</table>
Audit Standards:

1. All infants meeting the BAPM intensive care category, should have an admission blood pressure (BP) recorded.
2. Infants being treated for hypotension should have 15 minutely recordings of BP if not invasively monitored.
3. Infants should not receive a bolus of saline unless there is documented evidence to support a clinical suspicion of hypovolaemia.

1. Introduction:

Neonatal hypotension is usually the result of abnormal peripheral vasoregulation or myocardial dysfunction. Rarely is it due to hypovolaemia.

The definition of hypotension in neonates varies, the threshold for intervention and benefits of intervention are not well established to this day1,2,22. Hypotension has been associated with an increased likelihood of adverse outcomes3.

2. Definition of Hypotension:

Blood pressure (BP) is used as a marker of systemic perfusion however BP correlates only weakly with cardiac output.

2.1 Preterm neonates

Various definitions of hypotension are used in preterm infants including:
- a mean arterial blood pressure (MAP) below the 10th centile for gestation/birth weight and postnatal age4 (see Appendices 1 and 2)
- a MAP below an infant’s gestation age in weeks.

More recently severe hypotension in preterm neonates has been defined in some studies as a mean arterial pressure of 5mmHG or more below gestational age (minMAP≤GA-5). There is some evidence of greater benefit of intervention in this group22.

Tolerating isolated hypotension in a stable preterm neonate with no signs suggestive of poor perfusion is increasingly becoming commonplace1.

2.2 Term neonates

Hypotension in term neonates is less common and occurs due to a wider range of reasons than in preterm infants. Hypotension in term neonates is less well studied than in preterm neonates. Isolated hypotension is uncommon in term neonates thus permissive hypotension in term babies is not a common consideration.

2.3 First 48-72 hours of life (transition period)

Values below the third percentile of mean blood pressure in the first 72 hours approximate the gestational age in weeks for an averagely sized infant5. In the presence of a large patent ductus arteriosus (PDA), the mean blood pressure
may be reduced significantly, in which case the systolic blood pressure may be a more accurate marker of the baby's cardiovascular stability.

2.4 After the first 48-72 hours of life (post transition period)
Values for gestational age are as below (see also Appendices 1\(^4\) and 2\(^6\)).

<table>
<thead>
<tr>
<th>Corrected Gestational Age (wks)</th>
<th>Systolic Blood Pressure (mmHg)</th>
<th>Mean Blood Pressure (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>23-26</td>
<td>35-45</td>
<td>30</td>
</tr>
<tr>
<td>27-32</td>
<td>40-55</td>
<td>35</td>
</tr>
<tr>
<td>33-36</td>
<td>45-55</td>
<td>40</td>
</tr>
<tr>
<td>37-42</td>
<td>55-65</td>
<td>45</td>
</tr>
</tbody>
</table>

3. Measurement of Blood Pressure

Oscillometric cuff measurement may overestimate blood pressure in hypotensive preterm newborns\(^7,8\) therefore if unwell or intervention is being considered insertion of an arterial line should be considered being wary of the associated and significant risks of their use\(^9,10,11\).

An appropriately sized cuff should be used with the infant supine, when the infant is settled and with the arm at the level of the right atrium.

Transduced intra-arterial blood pressure monitoring systems need to be interpreted with care:
- Damping can occur due to the small diameter catheter, partial occlusion by the vessel wall or the presence of air bubbles\(^12\)
- Use of a pedal artery may cause systolic pressure to appear higher than when measured by a central catheter\(^13\)
- The position of the transducer should be level with the heart
- The arterial line should be re-zeroed before acting on a hypotensive reading

4. Risk Factors for Hypotension

- Prematurity
- Positive pressure ventilation (particularly with high mean airway pressures and HFOV)
- Large Patent Ductus Arteriosus – ductal steal can reduce MAP and coronary artery blood flow
- Lack of antenatal steroids prior to delivery
- Sepsis
- Haemorrhage – eg APH, cord prolapse, twin to twin transfusion syndrome, large intracranial haemorrhage, large pulmonary haemorrhage
- Congenital cardiac disease
- Adrenal insufficiency
- Surgical intervention
- Hypoxic ischaemic encephalopathy (HIE)
- Persistent Pulmonary Hypertension of the Newborn (PPHN)
- Drugs – e.g. morphine infusions, maternal labetalol treatment

5. Complications of Hypotension\textsuperscript{4,15,16}

- Intraventricular haemorrhage
- Periventricular leukomalacia
- Long term neurological impairment
- End-organ dysfunction

6. Diagnosis

6.1 Clinical Assessment

Signs and symptoms of inadequate tissue perfusion may include:

- Urine output <1ml/kg/hr
- Central capillary refill >3 seconds (a poor indicator alone but useful if associated with other features)
- Base deficit >5
- Lactate >2mmol/L
- Pallor
- Tachycardia
- Cold extremities
- Weak pulses (femoral palpation best in hypotensive infants\textsuperscript{14})
- Apnoea and bradycardia
- Low blood pressure for gestational age

6.2 Monitoring

Infants with hypotension should ideally be monitored closely:

- Continuous monitoring of mean arterial pressure (if arterial access available)
- Cuff BP set to 15minute readings which are recorded (if arterial access not available)
- Continuous heart rate and saturation monitoring
- Central capillary refill time
- Urine output
- Core-peripheral temperature gap (>2°C is abnormal)
- Regular blood gas/lactate monitoring

6.3 Echocardiography

Echocardiography (if expertise is available) may detect the presence of:

- PDA which may be contributing to hypotension
- Pulmonary hypertension (PPHN)
- Poor cardiac contractility
- Congenital cardiac disease

6.4 Consider contributing causes and intervention

- Blood loss/hypovolaemia
- Pneumothorax
- Sepsis
- PDA\textsuperscript{18}
- High mean airway pressure compromising venous return to the heart
- Adrenocortical insufficiency\textsuperscript{19,20}

7. Management of Hypotension:

Not intervening in babies with isolated hypotension and no signs of cardiovascular compromise remains reasonable. Intervention should be considered particularly in infants with clinical evidence of poor perfusion associated with hypotension or those with isolated severe hypotension (minMAP≤GA-5)\textsuperscript{22}.

Evidence of benefit is conflicting. Studies have shown that anti-hypotensive therapy in the extremely preterm neonate is independently associated with increased risk of death and neurodevelopmental impairment/developmental delay when controlling for risk factors known to affect those outcomes\textsuperscript{21}. Other studies have shown benefit of treating isolated hypotension\textsuperscript{22}.

7.1 Inotropes\textsuperscript{28,29,30,31,32}

*Dopamine* at lower doses (2-4 microgram/kg/mins) increases myocardial contractility and renal blood flow. At higher doses (10-20 microgram/kg/min) it increases vascular resistance. Dopamine is more effective than Dobutamine in the short term at raising the blood pressure in preterm infants, but this may not correlate with improving organ perfusion.

*Dobutamine* is a direct-acting inotropic agent which stimulates the ß-receptors of the heart and blood vessels causing increased cardiac output, vasodilation and reduced vascular resistance.

*Adrenaline* at low doses causes systemic and pulmonary vasodilation with an increase in the heart rate, stroke volume and contractility. Low doses of Adrenaline have been shown to be as effective as low/moderate doses of dopamine\textsuperscript{33,34}.

**Note:** High doses of both Adrenaline (≥ 500-600ng/kg/min) and Dopamine (≥ 15mcg/kg/min) can cause intense systemic vasoconstriction.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Category</th>
<th>Mode of Action</th>
<th>Haemodynamic Effect</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dobutamine</td>
<td>Inotrope</td>
<td>Beta adrenergic agonist</td>
<td>Enhanced myocardial</td>
<td>IVI 5-20 micro-grams/kg/minute</td>
</tr>
</tbody>
</table>
### Clinical Guideline: Management of Hypotension

#### Authors:
David Hopkins

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<table>
<thead>
<tr>
<th>Drug</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dopamine</strong></td>
<td><strong>Inotrope/vasopressor</strong> Alpha and beta adrenergic agonist <strong>Peripheral vasoconstriction Enhanced myocardial contractility and output</strong> IV 5-20 micro-grams/kg/minute</td>
</tr>
<tr>
<td><strong>Adrenaline</strong></td>
<td><strong>Inotrope/vasopressor</strong> Alpha and beta adrenergic agonist <strong>Enhanced myocardial contractility and output; peripheral vasoconstriction</strong> IV 100 nanograms/kg/minute – 1.5 micrograms/kg/minute</td>
</tr>
<tr>
<td><strong>Norepinephrine</strong></td>
<td><strong>Vasopressor</strong> Alpha( and beta) adrenergic agonist <strong>Peripheral vasoconstriction</strong> IV 20-100 nanograms/kg/minute Maximum 1 microgram/kg/minute</td>
</tr>
<tr>
<td><strong>Milrinone</strong></td>
<td><strong>Lusitrope</strong> <strong>Increases cAMP</strong> <strong>Increase myocardial contractility Decreases vascular tone in systemic and pulmonary arteries.</strong> Loading dose IV 50-75 micrograms/kg over 30-60 minutes then IV 30-45 micrograms/kg/hour</td>
</tr>
</tbody>
</table>

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**7.2 Volume expansion**

Volume expansion should be given only if there is significant clinical suspicion of hypovolaemia, increased capillary leak or blood loss. Giving fluid boluses can be counterproductive if there is an already poorly functioning myocardium or a PDA. Early use of Dopamine is more successful than colloid in increasing the blood pressure\(^{23}\).

As of yet there is insufficient evidence to determine whether infants with cardiovascular compromise benefit from volume expansion\(^{24}\) and extensive use is associated with significant untoward effects especially in preterm infants\(^{25}\).

10mls/kg of 0.9% sodium chloride should be given over 20-30 minutes if volume is chosen to treat hypotension\(^{26,27}\). Blood or Fresh Frozen Plasma should only be considered instead of sodium chloride if the baby is actively bleeding, thought to have lost significant blood volume or has deranged coagulation.

**7.3 Corticosteroids**

Adrenocortical insufficiency is becoming increasingly recognised as a cause of hypotension in preterm infants\(^{35,36,37}\). Adrenal corticoid insufficiency typically presents as severe refractory hypotension in preterm infants.

Hydrocortisone has been used successfully for treating refractory hypotension in preterm infants leading to stabilisation of blood pressure within 6-8 hours and to successful weaning from inotropes within 72 hours\(^{38}\). It is reasonable to consider use of hydrocortisone in infants who are still hypotensive despite treatment with dual inotropes.

Babies at highest risk are those:
- Under 30 weeks
- Under 14 days of age
- Concurrent perinatal stress (RDS, mechanical ventilation, surgery)

Blood cortisol levels can be useful in babies with refractory hypotension, if taken before giving hydrocortisone, and for assessing response to therapy. An unstimulated cortisol level <200nmol/L is suggestive of a degree of adrenal insufficiency. Whilst it is useful to have the cortisol level, the decision to start hydrocortisone should not depend on the result which may take hours.

An initial dose of Hydrocortisone 2.5mg/kg can be repeated at 4 hours if required, followed by 2.5mg/kg every 6 hours for 48hrs or until BP recovers. Then reduce treatment over at least 48hrs39.

7.4 Flow chart for management

The following flow chart is adapted from the Luton and Dunstable guideline40. There may be differences in the choice of dopamine or dobutamine as first line where the cause of hypotension is unknown depending on unit experience and preference.

The most recent Cochrane review of dopamine vs. dobutamine32 would suggest using dopamine as first line therapy based on the fact that it is more likely to result in an increase in blood pressure and if this fails the addition of dobutamine may be considered. The evidence that dopamine is more effective only extends as far as the short-term effect on blood pressure and there is an argument that dobutamine may be more likely to increase systemic blood flow.

If there is a significant PDA present or if there is echo evidence of cardiac dysfunction the use of dobutamine before dopamine may be more logical32.
Identify cause of hypotension
Echocardiography (where possible but do not delay treatment)
Consider: Pneumothorax, excessive MAP, haemorrhage

**Acute blood loss or hypovolemia**
- Volume expansion with 0.9% sodium chloride or blood. Begin with 10ml/kg
- If still hypovolaemic, give second bolus of sodium chloride or blood, otherwise consider treatment with dopamine

**Myocardial dysfunction/PPHN**
- Consider using dobutamine as first line
- Consider dopamine as second line
- Assess cardiac function, consider adrenaline or hydrocortisone

**Proven sepsis or NEC**
- Consider using dopamine as first line
- Consider treatment with adrenaline as second line
- Consider hydrocortisone

**Cause unknown/perinatal asphyxia**
- Consider dopamine or dobutamine as first line
- Add the other of dopamine/dobutamine depending on what already used first line
- Assess cardiac function, consider adrenaline or hydrocortisone
Appendix 1

<table>
<thead>
<tr>
<th>Hours postnatal age</th>
<th>3</th>
<th>12</th>
<th>24</th>
<th>36</th>
<th>48</th>
<th>60</th>
<th>72</th>
<th>84</th>
<th>96</th>
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<tr>
<td>500</td>
<td>36/23</td>
<td>36/24</td>
<td>37/25</td>
<td>38/26</td>
<td>39/28</td>
<td>41/29</td>
<td>42/30</td>
<td>43/31</td>
<td>44/33</td>
</tr>
<tr>
<td>600</td>
<td>36/24</td>
<td>36/25</td>
<td>37/26</td>
<td>39/27</td>
<td>40/28</td>
<td>41/29</td>
<td>42/31</td>
<td>44/32</td>
<td>45/33</td>
</tr>
<tr>
<td>700</td>
<td>36/24</td>
<td>37/25</td>
<td>38/26</td>
<td>39/28</td>
<td>42/29</td>
<td>42/30</td>
<td>43/31</td>
<td>44/32</td>
<td>45/34</td>
</tr>
<tr>
<td>800</td>
<td>36/25</td>
<td>37/26</td>
<td>39/27</td>
<td>40/28</td>
<td>41/29</td>
<td>42/31</td>
<td>44/32</td>
<td>46/33</td>
<td>46/34</td>
</tr>
<tr>
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<td>37/26</td>
<td>38/26</td>
<td>39/27</td>
<td>40/29</td>
<td>42/30</td>
<td>43/31</td>
<td>44/32</td>
<td>45/34</td>
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<td>40/28</td>
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<td>42/30</td>
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<td>1200</td>
<td>40/28</td>
<td>41/30</td>
<td>43/31</td>
<td>44/32</td>
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<tr>
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<td>40/28</td>
<td>41/30</td>
<td>43/31</td>
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<td>46/34</td>
<td>47/35</td>
<td>48/36</td>
<td>49/37</td>
<td>50/38</td>
</tr>
</tbody>
</table>

Fig. 2. Table of mean MBP and 10th percentiles by birthweight and postnatal age. The first figure is the mean MBP at the given weight and postnatal age and the second figure is the tenth percentile.


Appendix 2

![Mean Blood Pressure Changes within 7 Days: Infants without IVH (excluding times when colloid, dopamine and dobutamine support given)](image1)

Fig. 1. Mean blood pressure reference ranges for infants in the four birthweight groups during the first seven days of life. Inclusion and exclusion criteria are given in the text. Centiles displayed are 10th, 50th and 90th.

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1 Left hand column indicates weight in grams and mean blood pressure measured in mmHg
Reprinted from Early Human Development, 56, Cunningham S, Symon AG, Elton RA et al, Intra-arterial blood pressure reference ranges, death and morbidity in very low birthweight infants during the first seven days of life, Page 157, copyright (1999), with permission from Elsevier.2

References


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2 Blood pressure measured in mmHg
invasively measured blood pressure. *Acta Paediatrica*. February;94(2):191-6.[Ia]


