

## **HYPOTENSION**

### **Supporting information**

#### **What is the best method of measuring blood pressure in a neonate?**

There is currently no consensus on the best method in all cases (Goonasekera, 2000). Direct transducer readings through an umbilical line are commonly used in sick or very low birth weight neonates (Cordero, 2002), and are “widely accepted as the optimum method” (Dasgupta, 2003).

A combination of oscillometric and Doppler methods has been reported as providing better accuracy than each method on its own in a study in 174 term neonates (Nascimento, 2002). The use of a recently developed algorithm (SuperSTAT(R)) enabled non-invasive blood pressure measurement to comply with ANSI/AAMI accuracy standards ( $\pm 5$  mm Hg, SD  $\leq 8$  mm Hg) and to be comparable to invasive methods (Nelson, 2002). It is important that measurements are taken when the infant is in “a restful state” (not necessarily asleep) (Nwankwo, 1997). It is unclear whether indirect measurements taken from the calf are directly equivalent to those taken from the arm (Crapanzano, 1996; Kunk, 1996).

Cordero L, Timan CJ, Waters HH, et al. Mean arterial pressures during the first 24 hours of life in  $<$  or  $=$  600-gram birth weight infants. *J Perinatol* 2002;22:348-53

Crapanzano MS, Strong WB, Newman IR, et al. Calf blood pressure: clinical implications and correlations with arm blood pressure in infants and young children. *Pediatrics* 1996;97:220-4

Dasgupta SJ, Gill AB. Hypotension in the very low birthweight infant: the old, the new, and the uncertain. *Arch Dis Child Fetal Neonatal Ed* 2003;88:F450-F454

Goonasekera CD, Dillon MJ. Measurement and interpretation of blood pressure. *Arch Dis Child* 2000;82:261-5

Kunk R, McCain GC. Comparison of upper arm and calf oscillometric blood pressure measurement in preterm infants. *J Perinatol* 1996;16:89-92

Nascimento MC, Xavier CC, Goulart EM. Arterial blood pressure of term newborns during the first week of life. *Braz J Med Biol Res* 2002;35:905-11

Nelson RM, Stebor AD, Groh CM, et al. Determination of accuracy in neonates for non-invasive blood pressure device using an improved algorithm. *Blood Press Monit* 2002;7:123-9

Nwankwo MU, Lorenz JM, Gardiner JC. A standard protocol for blood pressure measurement in the newborn. *Pediatrics* 1997;99:E10

#### **Evidence Level: V**

#### **What is a normal blood pressure for a neonate, at term and preterm?**

“The normal physiologic blood pressure range ensuring appropriate organ perfusion in the neonate is unknown” (Seri, 2001). “Hypotension affects close to half of all ELBW infants, yet an agreement on its definition is still lacking” (Fanaroff, 2006). In low birthweight or preterm infants, the range of “normal” values is dependent on age in terms of weeks’ gestation and birthweight (Hegyí 1996; Hegyí 1994). New Zealand

guidelines (Knight, 2000) suggest that, for VLBW infants, “a good rule of thumb is to aim for the baby’s gestational age as the desired minimum mean blood pressure”. A postal questionnaire sent to all 120 neonatal ICUs in Canada (Dempsey, 2006), which had a 79% return rate (95 replies), found that 25.8% relied on blood pressure values as the sole criteria for intervention. A blood pressure less than gestational age in weeks was the most common trigger for treatment.

Dempsey EM, Barrington KJ. Diagnostic criteria and therapeutic interventions for the hypotensive very low birth weight infant. *J Perinatol* 2006;26:677-81

Fanaroff AA, Fanaroff JM. Short- and long-term consequences of hypotension in ELBW infants. *Semin Perinatol* 2006;30:151-5

Hegyí T, Carbone MT, Anwar M, et al. Blood pressure ranges in premature infants. I. The first hours of life. *J Pediatr* 1994;124:627-33

Hegyí T, Anwar M, Carbone MT, et al. Blood pressure ranges in premature infants. II. The first week of life. *Pediatrics* 1996;97:336-42

Knight D. Newborn Services Clinical Guidelines: Hypotension.  
<http://www.adhb.govt.nz/newborn/Guidelines/Cardiac/Hypotension.htm>

Seri I, Evans J. Controversies in the diagnosis and management of hypotension in the newborn infant. *Curr Opin Pediatr* 2001;13:116-23

### **Evidence Level: V**

#### **What is the role of clinical assessment (e.g. skin turgor, urine output) in deciding whether or not to treat at a specific blood pressure reading?**

No evidence can be identified with which to answer this question. There is general agreement that “decisions to treat hypotension should be based on the general condition of the infant, not on the mean arterial blood pressure alone” (Dasgupta, 2003), but no detail is given. Urine output is considered to be an unreliable indicator of hypotension (Dasgupta, 2003).

Dasgupta SJ, Gill AB. Hypotension in the very low birthweight infant: the old, the new, and the uncertain. *Arch Dis Child Fetal Neonatal Ed* 2003;88:F450-F454

### **Evidence Level: V**

#### **Should IV fluid be used as a first line for the treatment of hypotension? If so, what type and how much?**

Although hypovolaemia is a relatively uncommon cause of hypotension in the sick preterm infant, moderate fluid replacement is a reasonable precaution and so usually the first line treatment (Dasgupta, 2002). Two RCTs, in 63 (So, 1997) and 41 infants (Oca, 2003) respectively, have demonstrated that saline 0.9% is as effective as 5% albumin for treating neonatal hypotension. Isotonic saline has the further advantages of being cheap, of carrying no infection risk, and of causing less fluid retention in the first 48 hours (So, 1997). A recommended amount to use is 10-20 ml/kg over 30 minutes (Dasgupta, 2002).

Dasgupta SJ, Gill AB. Hypotension in the very low birthweight infant: the old, the new, and the uncertain. Arch Dis Child Fetal Neonatal Ed 2003;88:F450-F454

Oca MJ, Nelson M, Donn SM. Randomized trial of normal saline versus 5% albumin for the treatment of neonatal hypotension. J Perinatol 2003;23:473-6

So KW, Fok TF, Ng PC, et al. Randomised controlled trial of colloid or crystalloid in hypotensive preterm infants. Arch Dis Child Fetal Neonatal Ed 1997;76:F43-F46

### **Evidence Level: II**

#### **Should dopamine remain the first line drug treatment?**

A Cochrane review of 5 RCTs (Subhedar, 2003) concluded that dopamine was more successful than dobutamine for short-term treatment of hypotension, with fewer infants having treatment failure (RD -0.23; 95% CI -0.34 to -0.13). There was, however, no difference in mortality and no data on long term benefit or safety.

Subhedar NV, Shaw NJ. Dopamine versus dobutamine for hypotensive preterm infants. The Cochrane Database of Systematic Reviews 2003, Issue 3. Art. No.: CD001242

### **Evidence Level: I**

#### **What is the role of dobutamine?**

Dobutamine is generally used as a second line drug, in patients unresponsive to dopamine (Dasgupta, 2003). A range of doses from 5-20 mcg/kg/min has been used, and there is no clear evidence as to which of these is “correct” (Subhedar, 2003). New Zealand guidelines (Knight, 2000) suggest starting at the lower dose and increasing incrementally to the higher, after the dopamine dose has been increased to 10-20 mcg/kg/min without response.

Dasgupta SJ, Gill AB. Hypotension in the very low birthweight infant: the old, the new, and the uncertain. Arch Dis Child Fetal Neonatal Ed 2003;88:F450-F454

Knight D. Newborn Services Clinical Guidelines: Hypotension.  
<http://www.adhb.govt.nz/newborn/Guidelines/Cardiac/Hypotension.htm>

Subhedar NV, Shaw NJ. Dopamine versus dobutamine for hypotensive preterm infants. The Cochrane Database of Systematic Reviews 2003, Issue 3. Art. No.: CD001242

### **Evidence Level: II**

#### **What is the role of adrenaline (epinephrine)?**

A Cochrane review (Paradisis, 2004) identified only one on-going randomised study comparing adrenaline (epinephrine) with dopamine and this indicated that both agents significantly increased heart rate and mean BP, with no statistically significant effect on left or right ventricular outputs. No other outcomes were reported. The review concluded that there was insufficient data to make any recommendations, and called for larger trials to be carried out.

A retrospective “chart review” in 31 very low birthweight infants not responding to dopamine (Heckmann, 2002) found that the mean arterial blood pressure ( $=7$  (-1 to 13) mmHg,  $p=0.000001$ ) and the heart rate ( $+10$  (-10 to 42) bpm,  $p=0.000036$ )

increased significantly in all cases in response to a continuous infusion of adrenaline (epinephrine) in doses of 0.05-2.6 mcg/kg(-1)/min within the first 24 hours. No decrease in urine output was recorded. An increase in metabolic acidosis was noted as a potential adverse effect.

Heckmann M, Trotter A, Pohlandt F, et al. Epinephrine treatment of hypotension in very low birthweight infants. *Acta Paediatr* 2002;91:566-70

Paradis M, Osborn DA. Adrenaline for prevention of morbidity and mortality in preterm infants with cardiovascular compromise. *The Cochrane Database of Systematic Reviews* 2004, Issue 1. Art. No.: CD003958

## **Evidence Level: I**

### **What is the role of steroids?**

A single dose of steroids as rescue therapy is successful in “most babies” (Dasgupta, 2003). A randomised, double-blind, controlled trial in 20 premature infants not responding to dopamine and receiving adrenaline (epinephrine) infusion (Gaissmaier, 1999) found that 5/8 given dexamethasone (0.25 mg/kg) vs 1/9 given placebo (3 were excluded) were able to discontinue adrenaline (epinephrine).

A randomised comparison between dopamine and hydrocortisone in 40 very low birthweight infants (Bourchier, 1997) found the two treatments broadly equivalent in efficacy.

A retrospective review of 21 preterm infants given hydrocortisone as rescue therapy (Seri, 2001) noted a rapid increase in blood pressure (from 29.3 +/- 4.1 to 34.1 +/- 5.2 after 2 hours, rising to 41.8 +/- 6.6 mmHg after 6 hours).

Steroids may also have a role in the prevention of hypotension in preterm infants with low cortisol levels (Subheddar, 2003).

A Cochrane systematic review (Subheddar, 2007) concluded that in view of the scanty evidence for benefit and lack of long-term safety data, dexamethasone could not be recommended for routine use in preterm hypotension.

Bourchier D, Weston PJ. Randomised trial of dopamine compared with hydrocortisone for the treatment of hypotensive very low birthweight infants. *Arch Dis Child Fetal Neonatal Ed* 1997;76:F174-F178

Dasgupta SJ, Gill AB. Hypotension in the very low birthweight infant: the old, the new, and the uncertain. *Arch Dis Child Fetal Neonatal Ed* 2003;88:F450-F454

Gaissmaier RE, Pohlandt F. Single-dose dexamethasone treatment of hypotension in preterm infants. *J Pediatr* 1999;134:701-5

Seri I, Tan R, Evans J. Cardiovascular effects of hydrocortisone in preterm infants with pressor-resistant hypotension. *Pediatrics* 2001;107:1070-4

Subheddar NV. Treatment of hypotension in newborns. *Semin Neonatol* 2003;8:413-23

Subheddar NV, Duffy K, Ibrahim H. Corticosteroids for treating hypotension in preterm infants. *Cochrane Database of Systematic Reviews* 2007, Issue 1. Art. No.: CD003662

## **Evidence Level: II**

### **What are the best parameters for assessing hypovolaemia in the neonate?**

Hypovolaemia is uncommon and also difficult to diagnose in the sick preterm infant, due to the unreliability of indicators such as urine output and capillary refill time (Dasgupta, 2003). In view of the danger of excessive volume expansion (Ewer, 2003), it has been suggested (Evans, 2003) that echocardiography should be used to define systemic blood flow.

Dasgupta SJ, Gill AB. Hypotension in the very low birthweight infant: the old, the new, and the uncertain. *Arch Dis Child Fetal Neonatal Ed* 2003;88:F450-F454

Evans N. Volume expansion during neonatal intensive care: do we know what we are doing? *Semin Neonatol* 2003;8:315-23

Ewer AK, Tyler W, Francis A, et al. Excessive volume expansion and neonatal death in preterm infants born at 27-28 weeks gestation. *Paediatr Perinat Epidemiol* 2003;17:180-6

### **Evidence Level: V**

### **What is the maximum dose of dopamine, dobutamine and adrenaline (epinephrine) in neonatal hypotension?**

The maximum dose of both dopamine and dobutamine is 20 mcg/kg/min (Subhedar, 2004; Osborn, 2002; Knight, 2000). The maximum dose of adrenaline (epinephrine) is 0.5 mcg/kg/min (Paradisis, 2004; Knight, 2000).

Knight D. Newborn Services Clinical Guidelines: Hypotension. 2000.  
<http://www.adhb.govt.nz/newborn/Guidelines/Cardiac/Hypotension.htm>

Osborn D, Evans N, Kluckow M. Randomized trial of dobutamine versus dopamine in preterm infants with low systemic blood flow. *J Pediatr* 2002;140:183-91

Paradisis M, Osborn DA. Adrenaline for prevention of morbidity and mortality in preterm infants with cardiovascular compromise. *The Cochrane Database of Systematic Reviews* 2004, Issue 1. Art. No.: CD003958

Subhedar NV, Shaw NJ. Dopamine versus dobutamine for hypotensive preterm infants. *The Cochrane Database of Systematic Reviews* 2003, Issue 3. Art. No.: CD001242

### **Evidence Level: I**

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