

# Newborn Critical Care Center (NCCC) Clinical Guidelines

## Treatment of Hypotension for Extremely Low Birth Weight Infants

### BACKGROUND

In extremely low birth weight infants (ELBWs), hypotension within the first 24 hours after birth is most commonly caused by the premature infant's inability to properly transition to extra-uterine life, marked by immaturity of the myocardium. Other contributing factors may include anemia, adrenal insufficiency, a patent ductus arteriosus, and less commonly, hypovolemia. The incidence of hypotension increases with decreasing gestational age.

Hypotension has been associated with brain injury, NEC, ROP, and death. However, treatment with antihypertensive medications within the first 24 hours of life has also been associated with death and developmental impairment at 18-22 months adjusted age, even when adjusted for infant's clinical illness. Other studies have suggested that treatment of isolated hypotension has been associated with a higher rate of survival without major morbidity and a lower rate of severe cerebral abnormalities when compared to no treatment in risk-matched groups. The ongoing Management of Hypotension in Preterm Infants (HIP Trial) may provide clearer evidence.

### DEFINITION OF HYPOTENSION

Uncertainty persists regarding the 'normal' values for blood pressure and which treatment thresholds should be used. As a general guideline, within the first 72 hours, the lowest value for 'normal' mean arterial pressure (MAP) will be equivalent to the gestational age (GA) in weeks (ex: for a 25 week infant ~ normal MAP 25 mmHg). However, these are general guidelines and should always be considered in the context of other potential clinical indicators of systemic hypotension.

### EVALUATION

Central blood pressure monitoring (i.e. an umbilical arterial line) is the gold standard and generally treatment decisions should be based on these UAC measurements rather than cuff blood pressure measurements. Assessment of cardiac contractility and filling volumes by echocardiography may also assist in decision-making.

### MEDICAL TREATMENT OPTIONS

**Dobutamine** stimulates an increase in heart rate (chronotropy) and contractility (inotropy), allowing for more effective pumping. The increase in cardiac output makes dobutamine a good choice for neonates with myocardial dysfunction.

**Dopamine** increases the mean arterial pressure to improve peripheral and renal perfusion. Decreasing pulmonary vascular resistance makes dopamine an optimal choice when treating hypotension associated with persistent pulmonary hypertension.

## ALGORITHM DURING THE FIRST 24 HOURS OF LIFE

1. *If the MAP is less than the greater of [18 or  $\leq$ GA minus 5 mmHg] in asymptomatic infants or there is evidence of hypoperfusion (prolonged cap refill, lactic acidosis, etc.) – consider treatment with a single bolus of lactated ringer solution or normal saline (10 mL/kg). Also consider blood loss and the need for blood products for volume expansion. If the blood pressure does not increase, see below for recommended vasopressor treatment.*
2. *In asymptomatic infants, if the MAP is between the greater of [18 or GA minus 5 mmHg] and the normal MAP based on GA: may observe for at least one hour before considering treatment.*
  - a. *If the MAP is rising by at least 1 mmHg/hr, may continue to observe.*
  - b. *If the MAP is not increasing at this rate, consider treatment with a single bolus of lactated ringer solution or normal saline or blood products (as described above); if unresponsive, see below for recommended vasopressor treatment.*

### Vasopressor Treatment:

1. Begin vasopressor treatment with dobutamine or dopamine at an infusion rate of 5 mcg/kg/min; increase in increments of 2 mcg/kg/min every 15 minutes (consider increasing more aggressively for severe hypotension) until a MAP > GA is achieved or a dose of 15 mcg/kg/min is reached.
2. If MAP < GA on a single vasopressor agent infusion of 15 mcg/kg/min, begin a second agent (dopamine or dobutamine) infusion at 5 mcg/kg/min; increase in increments of 2 mcg/kg/min every 15 minutes (consider increasing more aggressively for severe hypotension) until a MAP > GA is achieved or a dose of 15 mcg/kg/min is reached.
3. If MAP < GA on 15 mcg/kg/min of both dobutamine and dopamine, administer a test dose of hydrocortisone. If the MAP increases within 6 hours, begin continuing doses of hydrocortisone. Please refer to the [Hydrocortisone Stress Dose Guidelines](#).
4. If the MAP does not respond to these therapies, consider echocardiography to further characterize the pathology.
5. If MAP > GA, treatment is not indicated unless accompanied by objective evidence of shock. In this case, first and second line vasopressor agents may be increased to a maximum of 20 mcg/kg/min each.
6. Infrequently, an epinephrine infusion may be indicated in the ELBW population if MAP remains < GA on maximum infusions of dopamine and dobutamine as well as stress dose steroids. If used, the starting dose for an epinephrine infusion would be 0.1 mg/kg/min.

## ALGORITHM AFTER THE FIRST 24 HOURS OF LIFE

1. If MAP < GA, begin vasopressor treatment. Fluid administration is not indicated unless there is evidence of volume depletion.

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### References:

1. Batton, B. et al. Early blood pressure, antihypotensive therapy and outcomes at 18-22 months' corrected age in extremely preterm infants. Arch Dis Child Fetal Neonatal Ed. 2016; 3: 101.
2. Dempsey EM, et al. Management of Hypotension in Preterm Infants (The HIP Trial): A Randomised Controlled Trial of Hypotension Management in Extremely Low Gestational Age Newborns. Neonatology 2014; 105: 275-281.
3. Durrmeyer X. et al. Abstention or intervention for isolated hypotension in the first 3 days of life in extremely preterm infants: association with short-term outcomes in the EIPAGE 2 cohort study. Arch Dis Child Fetal Neonatal Ed. 2017; 102:F490-496.
4. Rios, DR, Moffet, BS, Kaiser, JR. Trends in pharmacotherapy for neonatal hypotension. J Pediatrics. 2014; 4: 165.
5. Watterberg KL, Shaffer ML, for The PROPHET Study Group. Cortisol concentrations and apparent serum half-life during hydrocortisone therapy in extremely low birth weight infants. PAS 2005; 57: 1501.
6. Wong, JJ et al. Inotrope use among extremely preterm infants in Canadian neonatal intensive care units: variation and outcomes. Am J Perinatol. 2015; 1: 32.