**IV. Cardiovascular Support and HIE**

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**I. What is the goal Mean Arterial Blood Pressure (MAP) for infants with HIE?**

Blood pressure must remain in a safe range post HIE with the goals of avoiding hypotensive associate cerebral ischemia while ensuring the infant is not hypertensive with subsequent intra-cerebral hemorrhage. The ideal MAP for *term* infants with HIE has not been established. Since infants operate over a narrow blood pressure range, and hypoxic-ischemia impairs cerebral autoregulation, it is recommended to maintain MAP within the critical margin of **40mmHg to 60mmHg** [1] unless the hemodynamics suggest a more optimal MAP.

*Recommendations:*

1. Attempt to maintain MAP between 40mmHg and 60mmHg. Cerebral oximetry may be used to identify the optimal blood pressure for the patient.

2. Infants with pulmonary hypertension may require a MAP on the -higher end of this scale

3. Attempt to avoid acute fluctuations in blood pressure

*Level of Evidence:* V- Expert opinion based on current review of literature.

**II.** **What is the optimal method to manage hypotension with HIE?**

There is minimal documentation regarding the ideal method to augment MAP for infants with HIE. If there is clinical or historical evidence of hypovolemia (i.e. severe anemia, placenta abruption, cord compression) than volume may be indicated. The unwarranted use of fluids may exacerbate cerebral edema [2].

A 2002 Cochrane systemic review evaluating **Dopamine** for the prevention of morbidity and mortality with HIE was found to be inconclusive [3]. Further, Dopamine may not be the ideal first line agent for infants with evidence of pulmonary hypertension (PPHN) and HIE because it increases both systemic (SVR) and pulmonary vascular resistance (PVR) [4]. **Dobutamine**, at high doses, can also increase pulmonary artery pressure while reducing afterload and therefore would not be an ideal agent for infants with HIE and PPHN [5].

**Epinephrine**, at low to moderate dosing, will increase SVR with little effect on PVR. In addition, epinephrine can improve myocardial perfusion and dysfunction. Infants with HIE and PPHN, epinephrine may be the optimal choice for blood pressure augmentation [4].

**Milrinone** increases myocardial contractility and acts as a vasodilator (systemic and pulmonary). Infants with myocardial dysfunction, Milrinone may be a superior agent to improve contractility ensuring MAP is within target range prior to its initiation [6, 7].

*Recommendations:*

1. If infant is hypotensive, start treatment with a pressor which supports the clinical need of the neonate.

2. Obtain an Echocardiogram to assist in management. If myocardial dysfunction is evident on echocardiogram, consider the addition of epinephrine.

3. This is the recommended approach for hypotensive, encephalopathic infants *with or without* PPHN. Of note, the addition of Milrinone as a single agent may be beneficial in PPHN when normotensive or a combination of Milrinone with low dose epinephrine to prevent systemic hypotension with Milrinone infusion or if the patient had hypotension and PPHN [6, 7].

4. In the case of refractory hypotension to pressor support, consideration should be given to the addition of steroids with hydrocortisone the steroid of choice. Consider checking serum cortisol prior to starting hydrocortisone.

5. A majority of neonates with HIE do not have acute volume or blood loss. Unless there is a history of volume or blood loss, caution should be used in volume expansion for hypotension given the risk of cerebral edema and renal insufficiency due to hypoxic-ischemic injury.

*Level of Evidence:* IV- Case Series and Expert opinion based on current review of the literature.

**III. How does hypothermia affect hemodynamic status post asphyxia?**

Mild systemic hypothermia in itself appears to have minimal clinical effects on hemodynamic status. The CoolCap Trial which utilized mild systemic hypothermia to a rectal temperature of 34.5°C did not demonstrate affects on arterial blood pressure or initial treatment with inotropes or volume in infants with moderate to severe HIE [8]. In the NICHD whole body hypothermia trial, there were no differences in the incidence of pulmonary hypertension or cardiac arrhythmias between the treatment and controlled groups. However, there was a trend towards an increase use of inotropes in the hypothermia group [9]. In addition, the TOBY Trial did not find any significant difference in the incidence of hypotension, cardiac arrhythmias or pulmonary hypertension between hypothermic and normothermic infants [10].

*Level of Evidence:* IA- Based on Randomized Controlled Trials.

**VI. When should an echocardiogram be obtain for infants with HIE?**

We recommend an Echocardiogram be performed in any infant with HIE. Echocardiogram may be repeated and used to guide therapy in the following clinical scenarios:

1. Elevated cardiac enzymes if performed at your center

2. Clinical evidence of cardiac dysfunction

3. Clinical evidence of pulmonary hypertension

4. Hypotension (MAP < 40mmHg)

5. Requiring inotropic support

*Level of Evidence:* V- Expert opinion based on current review of literature.

**V. Should serum markers of cardiac injury be obtained in infants with HIE, what**

**markers, and when should they be obtained?**

Myocardial dysfunction is often the direct cause of perinatal brain injury. Myocardial damage may be clinically occult with mild HIE or manifest as a systemic hypoperfusion state in the cases of moderate to severe HIE. Serum cardiac markers may assist in injury detection and guide clinical management. Recent evidence suggests cardiac Troponins are superior to other markers of myocardial injury (LDH, CK, CK-MB) in detecting earlier, cardiac specific injury [11, 12].

**Cardiac Troponin T (cTnT)** and I (cTNI) are structural cytoplasmic proteins of myosites and the most cardiac specific of the troponins in the neonatal period [13]. Further, there is only one commercially available assay for Troponin T making standardization between different studies and reference ranges relatively consistent. Although there is not an accepted normal range for cTnT in neonates, a value of **≥ 0.1 ng/ml** in the setting of HIE has been considered as elevated in several studies and as a potential indicator of mortality in the neonatal period [11-14].

*Recommendations:*

1. If performed at your center and clinically indicated, obtain an ECG and Echocardiogram if cTnT or cTNI is ≥ 0.1ng/ml to evaluate myocardial

ischemia and cardiac function.

1. As stated above, Cardiac Troponin T or Troponin I may also be predictive of outcome and may aid the bedside clinician with additional prognostic information.

*Level of Evidence:* IIC- based on outcome data and case-controlled studies.

**VI. How should bradycardia associated with hypothermia be managed?**

Relative bradycardia **(70-100 bpm)** is not an uncommon occurrence in infants undergoing hypothermia. However, pathologic bradycardia can be a result of cardiac dysfunction, arrhythmias, deep hypothermia and increased intracranial pressure. Clinical intervention should be initiated when bradycardia is associated with evidence of decreased cardiac output, electrolyte abnormalities, elevated cardiac enzymes, and/or ECG abnormalities.

*Recommendations:*

1. If heart rate is <70bpm with evidence of reduced cardiac output (worsening metabolic acidosis, ↑lactic acid, prolonged capillary refill time, diminished pulses, low or borderline low MAP) obtain electrolytes including ionized calcium, ECG, echocardiogram, and ensure core temperature is appropriate.

2. If heart rate is <70bpm but >60bpm *without* evidence of reduced cardiac output, normal electrolytes, normal ECG and echocardiogram then close clinical observation is a reasonable approach.

3. The bedside clinician may consider decreasing sedation or rewarming by 0.50C to see if the HR increases if below 60 or below 70 with evidence of reduced cardiac output.

*Level of Evidence:* V- Expert opinion based on current review of literature.

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