Hypotension in the Neonate

Purpose and Goal: CNEP # 

- Learn about hypotension in the neonate.
- Learn about best practices for treating hypotension.

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Requirements for successful completion:

- Successfully complete the post-test
- Complete the evaluation form

Date

- December 2017 – December 2019
Learning Objectives

- Describe the pathophysiology of neonatal hypotension.
- Describe the risk factors for routine use of volume expansion.
- Describe at least 2 approaches for the treatment of neonatal hypotension.

Introduction

- Hypotension is common in preterm infants
  - It is less common in term infants
- There is no standard definition of hypotension
- Maintaining effective blood pressure is critical
- Untreated hypotension is associated with:
  - Significant morbidity
  - Significant mortality

Neonatal Hypotension

- Neonatal hypotension is a complex issue
- Hypotension by itself is not a pathologic condition
- It can be caused by several issues:
  - Hypovolemia
    - From fetal-to-fetal transfusion
    - From fetal-to-maternal transfusion
    - From an umbilical cord accident
  - Infection
  - Fetal arrhythmia
    - Leading to altered cardiac output
  - Maternal anesthesia
  - Pneumothorax
Asphyxia and hypoxemia
- Treatment of the underlying cause may improve blood pressure without any other intervention
- If a reversible cause cannot be found
  - Intervention should be timely
    - To avoid irreversible shock
    - To prevent possible death

Definitions of Hypotension
- There is no standard definition of hypotension
- Experts believe there are 3 levels of alteration
  - These can be used to refine the definition
    - Loss of blood flow autoregulation
    - Loss of vital organ function
    - Loss of tissue integrity
- Many unanswered questions remain re: pathology
- It is unclear how to determine BP parameters
  - That indicate pathology in each level
  - That lead to morbidity, mortality, or poor outcomes
- In general, two common parameters are used
  - During the first 3 days of life
    - A BP that falls below a MAP of 30
    - A MAP lower than the gestational age
  - During the neonatal period (greater than 3 days)
    - There is no consistent evidence
    - There are no “treatable” BP numbers
- The most accepted definition is:
  - The point at which autoregulation is lost
    - Leading to cerebral function compromise
    - Leading to tissue ischemia
- Despite a definition, BP remains the primary measure
  - BP indirectly measures several parameters:
• Cardiac stability
• Systemic blood flow
• Tissue and organ perfusion
• The challenge is to look at the entire clinical picture
  • Is there cardiovascular stability?
  • Are there abnormal indicators?
    • Abnormal pulses
    • Abnormal heart rate
    • Abnormal capillary refill
    • Abnormal acidosis
    • Abnormal oxygenation
    • Abnormal urine output
• A comprehensive assessment must be made

Pathophysiology of Hypotension

• Blood pressure is affected by several factors
  • Structure and function of myocardium
    • Ability of heart to pump blood
  • Elasticity of blood vessels
  • Circulating blood volume
  • Circulating blood viscosity
• The autonomic nervous system is important
  • In maintaining adequate organ perfusion
• The hemodynamic changes during transition are important
• Specific factors contributing to hypotension include:
  • Immature myocardium \( \rightarrow \) decreased contractility
    • Immature heart has less contractility
    • Immature heart cannot increase cardiac output
  • Transition from fetal circulation \( \rightarrow \) increased SVR
    • Maladaptation can easily occur
    • Immature heart cannot overcome resistance
• PDA → left to right shunt → ‘steal’ syndrome
  • A PDA causes decreased systemic blood flow
  • The PDA is open during systole and diastole
    • Creating a ‘steal’ syndrome
    • Which leads to decreased blood flow
• Perinatal hypoxia/asphyxia → neuroendocrine changes
  • A hypoxic insult leads to myocardial dysfunction
  • Hypoxia interrupts normal neuroendocrine changes
    • Which leads to a decrease in systemic blood flow
• Positive Pressure Ventilation → decreased venous return
  • Ventilation increases intrathoracic pressure
  • Which leads to decreased systemic blood flow
• Sepsis → inflammatory mediator release → vasodilation
  • Sepsis leads to release of inflammatory mediators
  • Inflammatory mediators lead to:
    • Peripheral vasodilation
    • Increased vascular permeability
    • Hypovolemia and hypotension
• Adrenal insufficiency → insufficient cortisol during stress
  • Preterm infants are at highest risk
    • Due to an immature adrenal gland
    • And limited ability to produce cortisol

Risks Associated with Hypotension

• Many studies show an association
  • Between hypotension
  • And poor neurodevelopmental outcomes
• Hypotension leads to impaired cerebral blood flow
  • Especially in preterm infants
  • Due to immature cerebral autoregulation
• Cerebral autoregulation is important
- Arteries constrict in response to increased pressure
- Arteries dilate in response to decreased pressure
- Cerebral autoregulation is critical to ensure constant blood flow
- Impaired autoregulation has been shown to be predictive
  - Of germinal matrix hemorrhage
  - Of intraventricular hemorrhage
  - Of periventricular leukomalacia
- The ability to autoregulate is immature in preterm infants
  - Making them more susceptible to ischemia
- Term infants are more tolerant of low blood pressures
  - Hypotension is more likely associated with
    - Sepsis
    - Asphyxia
    - Severe blood loss
    - Necrotizing enterocolitis
    - Persistent pulmonary hypertension

**Risks Associated with Volume Expansion**

- Many studies show problems associated with volume
- Extracellular body weight is elevated in the infant
  - As a percentage of body weight:
    - 60% at 20 weeks
    - 40% at 40 weeks
    - 20% in the adult
- Attempts to increase blood pressure through volume
  - Are frequently futile
  - May have adverse consequences
- The relationship between volume and BP is not straightforward
- Many studies show volume is not always beneficial
  - Administering fluid presumes low volume is the cause
  - Administering fluid can increase the incidence of IVH
• Administering fluid can also increase risks of:
  • BPD
  • NEC
  • PDA
  • Death
• Best practice is to evaluate the infant for adequate perfusion
  • Treatment should be based on perfusion status
  • As well as assessment of cardiac output
  • Treatment should not be based solely on blood pressure

Near-Infrared Spectroscopy or NIRS

• Methods for assessing cardiac output
  • Are limited in the neonatal population
    • Due to shunting through the PDA
    • Due to shunting through the PFO
• The use of ECHO to evaluate output is accurate
  • But not generally feasible
• The use of EEG to evaluate output is accurate
  • But not generally feasible
• Methods for assessing organ blood flow
  • Are being actively studied
  • Can help determine systemic blood flow
• NIRS is one method that is easily applicable
• NIRS helps determine blood flow
  • By measuring oxygen dependent compounds
    • That absorb light by passage through the brain
    • The compounds can be measured and calculated
  • Cerebral blood flow is measured using the calculations

Treatment of Hypotension
- The treatment of hypotension is controversial
- Hypotension should be treated based on the etiology
- The use of volume expansion is not generally recommended
  - The evidence for use of volume is insufficient
  - The evidence for best type of volume is insufficient
    - Blood
    - Albumin
    - Normal saline
    - Fresh frozen plasma
    - Plasma substitute
- The majority of infants are not hypovolemic
  - They have normal circulating blood volume
  - They would not benefit from volume expansion
- Studies show negative outcomes with routine use
  - Pulmonary
  - Cardiovascular
  - Gastrointestinal
  - Central nervous system
- The use of volume is indicated with evidence of blood loss
  - Evidence of blood loss includes:
    - Fetal anemia
    - Placenta previa
    - Placenta abruption
    - Umbilical cord accident
    - Fetal-Maternal transfusion
  - Effective circulating volume may be decreased
  - Volume expansion in this situation can:
    - Restore intravascular volume
    - Increase cardiac preload
    - Increase cardiac output
  - The administration of a volume expander
    - Normal saline
    - Ringers lactate
- O-negative blood
  - The initial dose should be 10 ml/kg over 5-10 minutes
    - This dose may be repeated as needed
    - Dopamine should be started at this point
- The use of Dopamine should be considered as first line therapy
  - Especially in premature infants
  - Especially when the etiology is unknown
  - Dopamine is the most commonly used inotropic drug
    - It is a naturally occurring endogenous catecholamine
    - Dopamine effects multiple systems:
      - Renal
      - Endocrine
      - Cardiovascular
      - Central nervous system
    - It exerts its effects by dose dependent stimulation of alpha- and beta-adrenergic and dopaminergic receptors
      - At low doses (2-4 mcg/kg/min) it dilates renal vessels
      - At moderate doses (5-10 mcg/kg/min) it increases both cardiac contractility and heart rate
      - At high doses (10-20 mcg/kg/min) it increases peripheral vascular resistance by peripheral vasoconstriction
    - Dopamine should be carefully titrated for optimum response
    - Dopamine is more effective than Dobutamine
      - It does not appear to affect the incidence of:
        - Tachycardia
        - Periventricular hemorrhage
        - Periventricular leukomalacia
    - Cautious stepwise increases are not associated with:
      - Abnormal neurological outcomes
      - Combined adverse outcomes
        - Death
        - Cerebral palsy
        - Developmental delay
• Severe neurodevelopmental delay
• The use of Dobutamine should be used with poor cardiac output
  • Especially in the first few days after birth
    • When peripheral vascular resistance is high
    • When an immature myocardium cannot pump against increased systemic resistance
• Dobutamine is a synthetic, relatively cardioselective inotrope that works on the alpha- and beta-adrenergic receptors
  • It increases cardiac contractility
  • It increases cardiac output
  • It is the treatment of choice for infants with myocardial dysfunction due to perinatal asphyxia
• Cautious stepwise increases are associated with:
  • Increased cardiac output
  • Increased systemic vasodilation
  • Improved systemic blood flow
• If hypotension increases after starting Dobutamine, low dose Dopamine may be added to the treatment plan
• The use of epinephrine should be considered with sepsis
  • Dopamine would remain the first line treatment
  • But epinephrine can help support cardiac function
    • Sepsis causes systemic vasodilation
    • Dopamine promotes vasoconstriction
    • Epinephrine promotes myocardial function
• Epinephrine is an endogenous catecholamine that is released by the adrenal gland in response to stressful stimulation
  • It has potent nonselective alpha-agonist action
  • It causes activation of beta-adrenergic receptors
  • It increases systemic vascular resistance
  • It increases cardiac output
  • At low doses (0.01-0.1 mcg/kg/min) it increases cardiac contractility and peripheral vascular resistance
- At higher doses (>0.1 mcg/kg/min) it causes peripheral vasoconstriction and increases systemic resistance
- Epinephrine causes disturbances in carbohydrate metabolism
  - Which can lead to increased hyperglycemia
- Cautious stepwise increases are not associated with:
  - Abnormal neurological outcomes
  - Combined adverse outcomes
    - Death
    - Cerebral palsy
    - Developmental delay
    - Severe neurodevelopmental delay
- The use of vasopressin *may* be helpful in neonatal shock
  - Vasopressin is an antidiuretic hormone
    - It is formed in the hypothalamus
    - Then secreted by the pituitary gland
  - It is used to treat vasodilatory shock
    - In adults and children
  - No large randomized controlled trial has been conducted in the neonatal population to date
- The use of milrinone is not currently supported
  - Milrinone is a selective phosphodiesterase III inhibitor
  - It exerts its effects by increasing cAMP
    - cAMP is cyclic adenosine monophosphate
    - Which is a derivative of adenosine triphosphate (ATP)
  - Which enhances cardiac contractility
    - Without raising myocardial O2 consumption
    - Without increasing cardiac afterload
  - Milrinone is increasingly being used in the NICU
    - To treat hypotension after cardiac surgery
    - To treat persistent pulmonary hypertension
    - As an adjunct to inhaled nitric oxide therapy
  - Studies have shown no adverse effects
    - Thrombocytopenia may be seen
• The use of hydrocortisone should be very limited
  • Hydrocortisone is as effective as Dopamine
  • It has been shown to improve:
    • Hypotension
    • Tissue perfusion
    • Risk of tissue ischemia
  • It exerts its effects by:
    • Upregulation of cardiovascular adrenergic receptors
      • Which leads to vasoconstriction
      • Which increases cardiac output
      • Which increases blood pressure
    • Upregulation of angiotensin II receptors
    • Inhibition of nitric oxide and prostaglandin actions
    • Inhibition of catecholamine metabolism
    • Increased intracellular calcium concentrations
• In general, information about long-term safety is lacking
• Poor neurodevelopmental outcomes have been noted
• Its use should be reserved for refractory hypotension
• Of note: hydrocortisone acts as a hormone replacement
  • Critically ill term and preterm infants lack cortisol
  • Cortisol levels are inversely related to gestational age
  • They also tend to be low in infants treated with inotropes
  • Hydrocortisone can be used to treat infants on Dopamine
  • It should not be used in conjunction with Indomethacin

Summary
• Maintaining effective blood pressure is critical
  • It is critical for adequate organ perfusion
  • It is critical for adequate tissue perfusion
• Many risks have been associated with hypotension
• Careful evaluation prior to starting treatment is important
  • Many treatments have negative side effects
Treatment of neonatal hypotension is multifactorial
  Success depends on treating the underlying cause

References


Evaluation

* Required fields

**Your information**

*Your name

*Your email address

*Your Seattle Children's ID

*Your hospital
  ☐ Seattle Children's Hospital
  ☐ Providence Regional Medical Center Everett
  ☐ Overlake Medical Center
  ☐ St. Joseph Medical Center
  ☐ St. Francis Hospital
  ☐ Harrison Medical Center
  ☐ Valley Medical Center
  ☐ Other Hospital, Medical Center, or Clinic

**Test**

- Neonatal hypotension can be defined as a mean arterial pressure or MAP less than gestational age in weeks.
  ☐ True
  ☐ False

- If an infant’s gestational age is 34 weeks, the mean arterial blood pressure should be at least 34 mm Hg.
• Measurements of cardiac stability in infants include heart rate, capillary refill time, urine output, and temperature.
  ○ True
  ○ False

• When treating hypotension, health care providers should be cautioned to treat a specific blood pressure number.
  ○ True
  ○ False

• If there is evidence of myocardial dysfunction, the next step is to administer dobutamine.
  ○ True
  ○ False

• The first line treatment for sepsis related hypotension is epinephrine.
  ○ True
  ○ False

**Evaluation**

We hope you found this educational offering both interesting and informative. We’d like to hear from you and appreciate you taking the time to answer these evaluation questions.

*Were you able to complete this activity in the allotted time?*
  ○ Yes
  ○ No

Were you informed of the following disclosures?
*Purpose of learning activity
  ○ Yes
  ○ No

*Requirements for successful completion of this CNE activity
  ○ Yes
  ○ No

*Presence or absence of conflict of interest of planning committee members
  ○ Yes
  ○ No

*Presence or absence of conflict of interest of content specialist(s)/author(s)/feedback person(s)
  ○ Yes
  ○ No

*Were your personal objectives successfully achieved?
  ○ Yes
  ○ Somewhat
  ○ No
If not, why not?

*What one thing might you do differently in your practice after this session?

Please evaluate the brief:

*Presentation organized
  ○ Excellent
  ○ Very good
*Materials offered relevant content
- Excellent
- Very good
- Good
- Fair
- Poor

*Assistance provided as needed
- Excellent
- Very good
- Good
- Fair
- Poor
- Not applicable

*Overall strength of presentation
- Excellent
- Very good
- Good
- Fair
- Poor

Stated objectives achieved?

*Describe the pathophysiology of neonatal hypotension.
- Excellent
- Very good
- Good
*Describe the risk factors for routine use of volume expansion.

*Describe at least 2 approaches for the treatment of neonatal hypotension.