Perinatal Depression

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Birth Asphyxia

- May occur in utero, during labor/delivery or during the neonatal period
- Condition of impaired blood gas exchange that leads to progressive hypoxemia and hypercapnia with metabolic acidosis.
- ACOG and AAP discourage the term "asphyxia" as imprecise
- Prefer the term “depression”

Birth Asphyxia

- The term birth asphyxia should be reserved for infants with four characteristics:
  - Profound metabolic or mixed acidemia (pH<7.0) on umbilical arterial blood sample
  - Persistence of an APGAR score of 0-3 for over 5 minutes
  - Neurologic manifestations in the immediate neonatal period incl seizures, hypotonia, coma or HIE
  - Evidence of multiorgan system dysfunction in the immediate neonatal period

Risk Factors – maternal

- Hypertensive disorders
- Cardiac disease
- Pulmonary disease
- Diabetes
- Sickle cell disease
- Renal disease
- Premature rupture of membranes
- Vaginal bleeding
- Severe anemia
- Rh/ABO sensitization
- Uterine or pelvic anatomic abnormalities
- Previous fetal or neonatal death

Risk Factors – fetal

- Multiple birth
- Post-dates
- IUGR
- Premature
- Polyhydramnios
- Meconium stained amniotic fluid

Risk Factors – Intrapartum

- Abnormal presentations
- Forceps (other than low)
- C-section delivery
- Prolapsed cord
- Abnormal heart rate or rhythm
- Prolonged general anesthesia
- Anesthetic complications (hypotension, hypoxia)
- Nuchal cord
- Prolonged or precipitous labor
- Uterine hypertonus
- Infection
Pathophysiology

Definitions
- Hypoxemia: low blood oxygen levels
- Hypoxia: lack of oxygen in the tissues of the body
- Ischemia: reduction or loss of blood flow to an organ

The fetus and neonate are more resistant to asphyxia than adults—good at redistributing preferentially, oxygenated blood to the heart, brain and adrenals.

Pathophysiologic sequence

- Can occur at any time, well defined series of events
- Onset of asphyxia results in period of rapid breathing followed by primary apnea
- Primary apnea is followed by irregular gasping and secondary apnea by 10 minutes
- Heart rate initially increases during the rapid breathing then falls along with the pH, BP and cerebral, pulmonary and renal perfusion.

- The infant’s response to resuscitation will depend on duration of the asphyxia
  - Will respond to stimulation if born during primary apnea
  - Will need PPV if delivered during gasping or secondary apnea

Pathophysiologic sequence

- As hypercapnia, hypoxemia and acidosis worsen, cerebral blood flow (CBF) becomes pressure passive which leaves the infant at risk of cerebral ischemia w/ systemic hypotension and cerebral hemorrhage with systemic hypertension.
- Prolonged asphyxia results in decreased cardiac output, hypotension and decreased CBF, risking cerebral ischemia and cell injury.
- As less oxygen is available anerobic metabolism ensues.

Systems Affected by Asphyxia

Neurologic
- Hypoxic – ischemic encephalopathy (HIE)
- Seizures
- Cerebral edema or hemorrhage

Cardiovascular
- Poor contractility– failure

Pulmonary
- Delayed onset of respirations→shunting→PPHN risk

Renal
- ATN→risk of failure
- Syndrome of Inappropriate Antidiuretic Hormone (SIADH)

GI
- Risk of NEC

Hematologic
- DIC

Metabolic
- Hypoglycemia, hypocalcemia, altered electrolytes
Hypoxic-Ischemic Encephalopathy

- During the insult as CBF falls below critical levels intracellular energy fails leading to decreased brain temperature and increased release of g-aminobutyric acid transaminase (GABA).
- This reduces the cerebral oxygen requirement and transiently minimizes the impact of the ischemia/asphyxia.

Hypoxic-Ischemic Encephalopathy (HIE)

- Neuronal death occurs in two phases after a reversible hypoxic-ischemic global insult:
  - First phase: immediate neuronal death related to cellular hypoxia and exhaustion of the cells energy stores
  - Second phase: 6+ hrs after insult delayed neuronal death occurs due to several mechanisms including: hyperemia, cytotoxic edema, mitochondrial failure, accumulation of toxins, nitric oxide synthesis and free radical damage (assoc w/ incr seizure activity and accounts for significant portion of final cell loss)

Assessment for HIE

- No particular lab test to rule HIE in or out
- Clinical presentation is the best indicator
- Degree of other system involvement, electrolyte abnormalities are dependent on the severity of the insult
- Sarnat and Sarnat’s 3 Clinical Stages of Perinatal Hypoxic Ischemic Brain Injury (1976)

Mild HIE

- Mildly increased muscle tone, brisk deep tendon reflexes during the first few days
- Transient behavioral abnormalities: poor feeding, irritability, irritated crying, sleepiness
- Normal CNS findings by 3-4 days of life

Moderate HIE

- Lethargic infant with significant hypotonia and decreased deep tendon reflexes
- Grasping, Moro and sucking reflexes sluggish or absent
- Occasional periods of apnea
- Seizures usually occur in the first 24hrs of life
- Full recovery in 1-2 weeks is possible and associated with a better long term outcome
Severe HIE

- Stupor or coma is typical
- Irregular breathing, generally requires vent support
- Hypotonia and depressed deep tendon reflexes
- Neonatal reflexes (sucking, Moro, etc) are absent
- Pupils can be dilated, fixed or poorly reactive to light
- Seizures occur early and often and may worsen over the initial hours of recovery secondary to reperfusion injury
- Fontanel may bulge with increasing cerebral edema
- HR and BP irregularities are common secondary to cardiorespiratory failure
- Multiple organ involvement common

HIE outcomes

- Dependent on severity
- Mild (Stage I) HIE—generally normal neurological outcome
- Moderate (Stage II) HIE—some with normal outcomes, resolution of neurological symptoms and normal nipple feeding by 1-2 wks is a good prognostic sign
  - 30-50% with serious long term complications (CP, mental retardation)
  - 10-20% with minor neurological morbidities

HIE Outcomes, cont

- Severe (Stage III) HIE
  - Mortality rate of 50-75%, most during the first month
  - 80% of the survivors develop serious complications: mental retardation, epilepsy, CP
  - 10-20% with moderately serious disabilities
  - Up to 10% are normal
  - One study showed school age children with a history of moderate to severe HIE but neurologically normal, 15-20% had significant learning disabilities

Management

- First goal is always prevention—identify infants at risk and be prepared
- Immediate resuscitation, NRP
- In the neonatal period:
  - Maintenance of adequate ventilation—hypercarbia can increase cerebral intracellular acidosis and impair cerebral vascular autoregulation
  - Maintenance of adequate oxygenation—PaO2>40 in preterm, >50 in term, avoid hyperoxia

Management, cont.

- In the neonatal period, cont.
  - Maintenance of adequate perfusion—maintain BP in the normal range for GA, volume and inotropes are often necessary, stable BP necessary with loss of cerebrovascular autoregulation
  - Correct metabolic acidosis—volume expanders are preferable to avoid risk of hypercarbia with bicarb
  - Maintain normal electrolytes and glucose—often hyper then hypoglycemic, hyponatremia common

Management, cont.

- In the neonatal period, cont.
  - Prevention of cerebral edema—avoid fluid overload. Often have to restrict fluids to 60ml/kg/d, can decrease to 50ml/kg/d.
  - Control of seizures—Phenobarbital is the first choice: loading dose of 20mg/kg IV. If unresponsive, 5mg/kg doses up to 40mg/kg.
  - If unable to control seizures with Phenobarbital start Ativan (lorazepam) 0.1mg/kg/dose—repeat as necessary to control.
**Seizures**

- Common with HIE
- Must be distinguished from
  - Jitteriness: usually normal eye movement, extremities are containable, fine movements
  - Benign myoclonic activity: nonrepetitive, isolated jerky movements, generally occur during sleep
- Consider other causes: metabolic disturbances (hypoglycemia/calcemia), inborn errors of metabolism, cerebral infarction, intracranial hemorrhage, infection (meningitis, TORCH, sepsis), neonatal drug withdrawal, developmental abnormalities

**Seizures, cont.**

- The earlier the onset the more ominous the prospects for recovery
- Important to recognize:
  - Seizure activity can further damage the brain
  - Suggestive of serious illness/injury which needs careful management
  - Subtle seizure activity requires astute observation
- Obtain EEG as soon as practical

**Seizures-- Pathophysiology**

- Neurons are depolarized by an inward migration of sodium
- They are repolarized by an efflux of potassium.
- Seizures occur due to excessive depolarization which results in excessive synchronous electrical discharge.

**Seizures-- Pathophysiology, cont.**

- Volpe (2001) proposed four possible reasons for the excessive depolarization
  - Failure of the sodium-potassium pump secondary to a disturbance of energy production.
  - Relative excess of excitatory vs inhibitory neurotransmitter.
  - Relative lack of inhibitory vs excitatory neurotransmitter.
  - Alteration in the neuronal membrane resulting in an inhibition of sodium movement

**Management**

- Assure adequate airway/ventilation
- Close CRM/oximetry monitoring
- Access for anticonvulsants
- Stat glucose, calcium, sodium and magnesium levels

**Selective Head Cooling**

- Research has shown that hypothermia can be neuroprotective
  - May modify cells programmed for apoptosis, leading to their survival
  - May protect neurons by reducing cerebral metabolic rate, attenuating the release of excitatory amino acids, lowering the production of toxic free radicals
- Have considered whole body cooling but adverse effects of core body temp of <34 degrees may outweigh the neuroprotective value of hypothermia
CoolCap Study Group

- 234 term infants with moderate to severe neonatal encephalopathy and abnormal EEG randomized to control or study group
- Head cooling was initiated within 6 hrs and continued x 72 hr when infant was gradually rewarmed
- Infants were cared for on a radiant warmer with temp adjusted to maintain rectal temp of 34-35 degrees
- CoolCap water temp started at 8-12 degrees
- Outcomes—no change in those with the most severe EEG changes, but beneficial to those less effected

Cochrane Review 2007

- Systematic review of eight randomized trials (n=638) found that therapeutic hypothermia is beneficial to term newborns with HIE
- Found that cooling reduces mortality without increasing major disability in survivors

Head Cooling Eligibility (Swedish Medical Center Protocol)

- Neonate ≥ 36 wk GA, ≥1800 gm BW & at least one of the following:
  - APGAR ≤ 5 at 10 min; cont need for PPV at 10 min of age; acidosis within 1st hr of life with umbilical cord pH or arterial pH < 7.0; base deficit ≥ 16 in cord blood or in 1st hr of life
  - Step 2: moderate to severe encephalopathy with altered state of consciousness & at least one of the following:
    - Hypotonia, abnormal reflexes, absent or weak suck, clinical seizures
  - Step 3: 20+min. EEG showing moderately/severely abnormal background activity or seizures

Selected References