

Neurologic problems in the neonate

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Hypoxic ischemic encephalopathy

Hypoxic ischemic encephalopathy refers to behavior and neurologic abnormalities exhibited by the newborn foal that cannot be attributed to an infectious disease, congenital or developmental malformation. This disorder is also known as neonatal encephalopathy, neonatal maladjustment syndrome or perinatal asphyxia syndrome. Hypoxic ischemic encephalopathy has been recognized in the neonate for several decades and is more correctly defined as a component of a broader term, hypoxic ischemic asphyxia syndrome (HIAS or HIS).

Foals present with a wide range of clinical signs including mild depression with loss of the suck reflex to grand mal seizure activity. Most individuals are normal at birth but show signs of central nervous system abnormalities within a few hours following birth. Occasionally the foal may be abnormal at birth or may not show clinically signs until 24 to 36 hours of age. Hypoxic ischemic encephalopathy is commonly associated with adverse intrapartum events including dystocia and premature placental separation. Often the foal has no history of adverse intrapartum events suggesting an unrecognized in utero event. Disorders of the neonatal period may cause hypoxic insult but are less often identified as a cause.

Most of our understanding of the pathophysiology of hypoxic ischemic asphyxia syndrome is taken from human medicine. The fetus responds to uterine asphyxia by redistributing cardiac output to the central organs-brain, heart and adrenal glands. If the hypoxic insult continues, a point is reached beyond which the fetus cannot maintain this centralization of circulation, cardiac output falls and cerebral circulation diminishes. The loss of oxygen results in a substantial decrease in oxidative phosphorylation in the brain with concomitant decreased energy production. The cell membrane pump cannot maintain the ionic gradients, and the membrane potential is lost in the brain cells. Calcium flows down its concentration gradient and into the cell resulting in cell damage by activation of calcium dependent proteases, lipases and endonucleases. Protein biosynthesis is halted and remains inhibited in specific areas of the brain and returns to normal in less vulnerable areas of the brain. A second wave of neuronal cell death occurs during the “reperfusion” phase and is thought to be similar to classically described “post-ischemic reperfusion injury” in that damage is due to production of and release of oxygen radicals, synthesis of nitric oxide and inflammatory reactions.

Although this discussion is limited to the neurologic manifestations of hypoxic disease, one should keep in mind that many systems are negatively impacted including the renal, gastrointestinal, cardiac, respiratory, hepatic and endocrine.

Therapy is multifactorial and includes control of seizures, general cerebral support, correction of metabolic abnormalities, maintenance of normal arterial blood gas values, maintenance of tissue perfusion, prevention of secondary infections, maintenance of renal function, treatment of gastrointestinal dysfunction and general supportive care. Initial therapy includes broad-spectrum antibiotics (penicillin and an aminoglycoside or cephalosporin), parental or enteral feeding, and appropriate supportive care (maintaining sternal recumbency if recumbent, keeping clean/dry, etc). Diazepam and phenobarbital are the most commonly used anti-convulsant medications. Cerebral perfusion is maintained by careful titration of intravenous fluids, neither too much nor too little, and the administration of inotropes and pressors to maintain adequate perfusion pressures. Often these foals have a variety of metabolic problems including hypo- or hyperglycemia, hypo- or hyperkalemia, hypo- or hypercalcemia, hypo- or hyperchloremia and metabolic acidosis. Intranasal oxygen insufflation is generally needed to support the foal because of the recurrent bouts of hypoxemia and occasional bouts of hypercapnia. Additional respiratory support may be needed including caffeine or mechanical ventilation. Other medications used in the treatment of hypoxic ischemic encephalopathy include DMSO, mannitol, naloxone, magnesium sulfate and thiamine. The efficacy of these drugs has not been proven. The average length of treatment is 5-7 days. The outcome of these foals is generally good unless secondary complications arise.

Bacterial meningitis

Bacterial meningitis often results from a generalized septicemia in neonates with failure of passive transfer, although it may be a primary entity. Clinical signs generally include depression, recumbency and seizure activity. Agents causing meningitis are similar to those that cause septicemia and include *E. coli* and *beta-hemolytic streptococcus*. Diagnosis is confirmed by cerebral spinal fluid analysis and culture. Treatment includes aggressive antimicrobial therapy and supportive therapy such as parental fluids, parental or enteral feedings, protection from injury, respiratory care and appropriate anti-convulsants. Antimicrobials should include those that penetrate the blood brain barrier such as 3rd generation cephalosporins. Prognosis is generally guarded.

Metabolic disturbances

Several metabolic disturbances can result in neurologic signs in the neonate including hypo- or hyponatremia, hypoglycemia and acid/base disorders. Hyponatremia secondary to gastrointestinal disorders or severe renal disease may result in central neurologic signs including a change in mentation and gait. In the neonate hyponatremia is common in those with a ruptured bladder. Hypoglycemia is often identified in neonates that are septic, although because the neonate has limited reserves, hypoglycemia may result from any disease or management error that limits energy intake. Clinical signs of marked hypoglycemia include profound depression or coma.

Hydrocephalus

Hydrocephalus may be congenital or acquired. It is most commonly caused by cerebral malformation and accumulation of excessive fluid in the ventricular spaces. Clinical signs can include enlarged and dome shaped head, changed mentation, and abnormal gait. No treatment exists and prognosis is hopeless.

Kernicterus

Kernicterus is an acute toxicity caused by bilirubin. Neurotoxicity results when unbound, unconjugated bilirubin enters the neurons and forms a deposit and irreversible damage. This acute toxicity can occur after a hemolytic crisis. Signs include a stiff gate, opisthotonus, tremors, head pressing, and propulsive walking. Signs may be permanent. Kernicterus is usually not seen until the bilirubin is in the mid to high 20's or 30's. The best treatment is prevention of severe hyperbilirubinemia before toxicity occurs. Prognosis is poor.

References

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