Neonatal hypoxia

Hypoxia is insufficient supply of oxygen to the organism or individual tissues, caused by a decrease in the oxygen tension in the arterial blood. Asphyxia is an interruption of the oxygen supply to the body, resulting in hypoxemia (decrease in pO_2) and hypercapnia (increase in pCO_2) and metabolic acidosis. It can turn into ischemia, or interruption of the supply of all substrates to tissues and organs, up to a complete stoppage of circulation.

Perinatal asphyxia is determined based on 4 criteria:

- severe metabolic or mixed acidosis (pH below 7.0; BE below −15[1] (−12)[2] from umbilical artery)
- Apgar score 0-3 for more than 5 min. after birth
- neurological symptoms in the early neonatal period (increased irritability, convulsions, hypotonia, coma)
- multi-organ systemic involvement in the early neonatal period (kidney, heart, liver involvement during the first 3 days of life)[3][1]

To pronounce the diagnosis, it is necessary to exclude other causes: trauma, coagulopathy, infections, genetic disorders.[2]

The incidence of perinatal asphyxia is 0.2-0.4% in full-term newborns, in low birth weight newborns it is 10x higher, up to 1/5 of asphyxiated babies die.[4]

The consequence of severe perinatal asphyxia is **hypoxic-ischemic organ damage** (HIE). The long-term neurological consequences are cerebral palsy (CP), mental retardation, epilepsy and difficulties at school.[1] The incidence of HIE is 2–9 per 1000 live births of full-term neonates, the mortality due to HIE is about 11 %.[2]

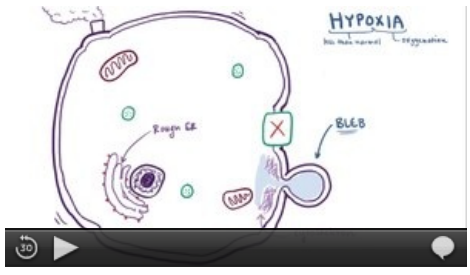
Despite the improvement of perinatal care, the incidence of cerebral palsy remains the same in the long term, namely 1-2 per 1000 live births of full-term newborns. 8-17% of cerebral palsy is due to asphyxia, but in most cases the cause remains unknown. 75% of children with cerebral palsy had normal Apgar scores.[2]

Causes

- **prenatal** (90 %):
  - interruption of blood flow through the umbilical cord (compression of the umbilical cord, right node), violation of gas exchange at the level of the placenta (abruption of the placenta, placenta praevia, placental insufficiency), perfusion disorder on the part of the mother (hypo- or hypertension (eclampsia), abnormal uterine contractions), hypoxia of the mother;
- **intrapartum**:
  - cephalopelvic disproportion, breech birth, meconium in amniotic fluid, umbilical cord prolapse, maternal infection, maternal diabetes mellitus, postmaturity, prematurity, IUGR;
- **postnatal**:
  - pneumopathy, congenital heart defects, congenital developmental defects, hereditary metabolic disorders (urea cycle disorders).[4]

Pathophysiology

The fetus and newborn are more resistant to asphyxia than adults. Hypoxia/asphyxia induces reflex organ redistribution of blood - **blood centralization** - oxygen and nutrients are preferentially delivered to the heart, brain and adrenal glands. Blood pressure, heart rate, and central venous pressure rise in an effort to maintain cerebral perfusion. Prolonged acidosis and hypercapnia leads to damage and necrosis of cells and thus to impairment of cerebrovascular autoregulation. With systemic hypotension there is a risk of cerebral ischemia, with systemic hypertension there is a risk of intracranial bleeding. After the end of the hypoxic insult, abnormal energy metabolism and low ATP levels persist (energy failure). Free radicals are formed, intracellular glutamate rises, cytosolic Ca^{2+} rises, delayed cell death occurs. During this period, nerve fibers disintegrate.[2]



Hypoxia (video).

Changes in vital signs during asphyxia:

- respiratory rate:
  1. first rises
  2. then falls (20 s) - primary apnea,
  3. the centers of the oblongata and pontus are disconnected and uncoordinated breaths occur - gasping (minutes),
  4. secondary apnea;
- heart action: rises and then falls;
- blood pressure: rises and then falls.[4]

Pathophysiology of asphyxia at the cellular level::

During hypoxemia, there is a transition to anaerobic metabolism - increased lactate production and the development of metabolic acidosis. Only 2 moles of ATP are produced from 1 mole of glucose. As a result of the failure of energy metabolism, there is a malfunction of ion pumps (Na/K, Ca) and a malfunction of voltage channels. Membrane depolarization develops and ions move (Na^+ and Ca^{2+} into cells, K^+ out of cells). Along with Na^+ and Ca^{2+}, water also moves into the cells, resulting in cell edema. Cell death occurs.[4] During **hypoxia**, xanthine oxidase predominates, which, during reperfusion, begins to excessively form free radicals.

After the end of asphyxia, there is a so-called **therapeutic window** (6 hours) – a period of reperfusion, the formation of oxygen radicals and the activation of inflammatory cells – which is followed by irreversible damage (activation of apoptosis).[4]

The vulnerability of the CNS changes with gestational age – in newborns up to the 34th week of pregnancy, the periventricular white matter is most affected (periventricular leukomalacia, PVL develops), in slightly immature and full-term newborns, it is the border of *a. cerebri anterior* and *media* and the border of *a. cerebri media* and *posterior*. As a result of multifocal ischemic cortical necrosis, PVL or intracranial hemorrhage, porencephaly, hydrocephalus, hydrancephaly, multicystic encephalomalacia may develop.[2]

Clinical picture

Symptoms of CNS damage in a full-term newborn: convulsions, abnormal breathing pattern (apnea), abnormal posture (hypertonia, hypotonia), pathological movements, poor sucking or absence of newborn reflexes, irritability.[2] The clinical picture of white matter necrosis in full-term infants is usually asymptomatic at first, neurological consequences appear only in infancy, diagnosis is sonographic.

Multi-organ damage

Cardiovascular system:

- hypotension, tachycardia;
- transient ischemia → transient tricuspid insufficiency;
- necrosis of the myocardium → myocardial dysfunction (poor contraction of the ventricles, it barely moves, contractility returns within 1-2 hours);
- congestive heart failure;
- evidence of cardiomegaly on X-ray; on the ECG, signs of myocardial ischemia with depression of the ST segment and inversion of the T wave, heart rhythm disorders; echocardiography reveals both right- and left-sided insufficiency (left-sided dysfunction is less frequent, right-sided dysfunction is characterized by a dilated P chamber and tricuspid insufficiency), evidence of PDA; laboratory markers: CK-MB, troponin-T.

Kidneys:

- oliguria or anuria;
- acute tubular necrosis, possibly cortical necrosis (hematuria, proteinuria);
- renal failure;
- laboratory markers: hyperkalemia, increased urea, creatinine, hematuria, proteinuria, beta-2-microglobulin in urine (tubular lesion marker).

Liver:

- increased values of ALT, AST, ammonia;
- reduced values of albumin, glycemia, coagulation factors.

Lungs: RDS, persistent pulmonary hypertension (PPHN), pulmonary apoplexy, shock lung.

GIT: paralytic ileus, in low birth weight newborns, the development of necrotizing enterocolitis (5-7 days under the picture of acute abdomen) up to bowel perforation and peritonitis.

Blood: DIC, thrombocytopenia.

Metabolism: acidosis (lactic), hypoglycemia (hyperinsulinism), hypocalcemia, hyponatremia/syndrome of inappropriate secretion of antidiuretic hormone (SIADH); myoglobinuria.

Adrenal glands: bleeding into the adrenal glands.

Skin: subcutaneous fat necrosis.[5][6][2]

Hypoxic-ischemic encephalopathy

HIE is a clinical-pathological entity that arises as a result of hypoxic-ischemic involvement of the CNS in a full-term newborn. An immature newborn does not yet have a developed cortex - paradoxically, he has a better chance.

Sarnat score → we evaluate – behavior, tone, reflexes

1st degree – increased irritability, more awake, hyperreflexia, semi-extended holding of lower limbs

- a very easy to recall Moore's reflex
- if it lasts 24-48h and then goes away → it should be fine

2nd degree - alternating behavior - lethargy with irritability

- reduced momentum or pathological stereotypes (e.g. boxing, cycling)
- alternating hypo and hypertonia, adduction of thumbs in fists, suction disorders
- bradycardia
- apnoeic pauses occur - this means that the stem is affected → considerable damage
- subside within 3-7 days - will be a little affected
- if it does not subside after more than 7 days - there will be symptomatology - cerebral palsy, mild brain dysfunction, ...

3rd degree – coma, hypo to atony, hyporeflexia

- not breathing, about 30% have intractable convulsions
- 50% die, 50% survive.[5][6]

CNS involvement in premature infants

- in premature infants, asphyxia causes intracranial hemorrhage (PIVH), periventricular leukomalacia (PVL), or both
- periventricularly there is a germinal matrix - rich in capillaries, vulnerable
- classification of intracranial bleeding according to USG:
  - **1st degree** – bleeding only into the germinal matrix (cyst under the ependyma), practically without consequences
  - **2nd degree** – bleeding into the lateral ventricle without its dilatation
    - ependymitis, hydrocephalus (a combination of ostr. and hypores.)
  - **3rd degree** – bleeding into the lateral ventricle with its dilatation
  - **4th degree** – intraventricular hemorrhage + intraparenchymatous hemorrhage
- leukomalacia - at the watershed areas - mainly in the places of anastomoses between the cortical and central CNS watersheds
  - the more mature the child, the closer it is to the cortex.[5][6]

Diagnosis

- quite difficult
- **anamnesis**
- **physical examination** – CTG – rhythm changes, blood flow, Apgar score
- **laboratory**: Acid–base balance from umbilical cord blood - we take it whenever it is risky
  - pH *a. umbilicalis* 7.15-7.25 asphyxia I degree
  - pH *a. umbilicalis* 7.05-7.15 asphyxia II. degrees
  - pH *a. umbilicalis* below 7.05 asphyxia III. degrees
  - a drop in pH, especially together with a drop in BE, is unfavorable prognostically - this means that the metabolic component is also involved in the acidosis and that it has been developing for a long time
  - from the acid–base balance values and the Apgar score, we can best assess the cause of asphyxia – if both the Agpar and pH values are reduced, the cause is probably prenatal; with low Agpar and normal pH, it will probably be perinatal causes
  - **lactate, AST, ALT, beta-2-microglobulin**;
- **EEG**, aEEG (amplitude-integrated EEG)
- **MRI** - the method of choice
- CT - several weeks apart
- auditory, visual and somatosensory evoked potentials,
- US - Doppler can measure flows in the anterior cerebral artery (ACA), medial cerebral artery (ACM), CNS structures
- SPECT, PET - little clinical benefit yet.[5][6][2]

Therapy

- CPR – ensure ventilation (normocapnia), oxygenation (normoxia, not hyperoxia) and perfusion (volume expansion in case of hypovolemia, circulatory support of catecholamine in case of hypotension);
- correction of metabolic acidosis (volume expansion, adequate provision of vital functions);
- maintenance of normoglycemia (correction of hypoglycemia);
- suppression of convulsions - the drug of choice is phenobarbital (possibly in combination with diazepam, lorazepam, phenytoin);
- prevention of cerebral edema – mild fluid restriction;
- monitoring of diuresis (renal dysfunction);
- minimal handling of the patient;
- thermomanagement – prevention of hyperthermia[2]
  - controlled hypothermia: 32-34°C for 72 hours

Sources

Related articles

- Cardiopulmonary resuscitation of the newborn
- Hypoxic-ischemic encephalopathy
- Diagnosis of fetal condition during pregnancy and delivery • Intrapartum fetal monitoring • Fetal hypoxia

External links

- Doporučený postup ČNeoS (2019): ŘÍZENÁ HYPOTERMIE V LÉČBĚ HYPOXICKO – ISCHEMICKÉ ENCEFALOPATIE (http://www.neonatology.cz/upload/www.neonatology.cz/Legislativa/Postupy/hie-a-rizena-hypotermie-revize-doporuceneho-postupu-27052019.pdf)

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