Sympathetico-adrenal System in newborn with Hypoxic-ischemic encephalopathy

Thesis
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By

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List of abbreviation

- **ACTH** : Adreno corticotropic hormone
- **AAP** : American academy of pediatric
- **ACOG** : American college of obstetric and gynecology
- **BUN** : Blood urea and nitrogen
- **cAMP** : Cyclic adenosine mono phosphate
- **CBF** : Cerebral blood flow
- **CNS** : Central nervous system
- **CRH** : Corticotropine releasing hormone
- **CTG** : Cardiotocogram
- **CT scan** : Computerized tomography
- **DNA** : Deoxy ribo nucleic acid
- **EEG** : Electro encephalogram
- **FFA** : Free fatty acid
- **FHR** : Fetal heart rate
- **GA** : Gestational age
- **GABA** : Gamma amino butyric acid
- **HIE** : Hypoxic ischemic encephalopathy

- **IVH** : Intra ventricular hemorrhage
- **IADH** : Inappropriate anti diuretic hormone secretion
- **MRI** : Magnetic resonance imaging
- **MRS** : Magnetic resonance spectroscopy
- **NST** : None stress test
- **NPO** : Nothing per os
- **PET** : Position emission tomography
- **PVL** : Peri ventricular leukomalacia
- **SPECT** : Single photon emission tomography
- **US** : Ultra sonography
- **VMA** : Vanill mandelic acid

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Introduction

Neonatal hypoxic ischemic encephalopathy (HIE) is an important clinical problem in infancy associated with neonatal mortality, morbidity and long term unfavorable neurodevelopmental outcome **(Kamel et al., ١٩٩٨).**

Perinatal asphyxia is a condition of impaired blood gas exchange, that if persists leads to progressive hypoxemia and hypercapnia with metabolic acidosis. (**Avery et al; ١٩٩٩).** Perinatal asphyxia causes neurological manifestations as hypoxic ischemic encephalopathy (HIE), and evidence of multi-organ system dysfunction **(Ancel et al; ١٩٩٥).** The incidence of hypoxic ischemic encephalopathy is about ٢-٩ in ١٠٠٠ in live term birth. The common causes includes interruption of umbilical circulation as in cord compression, inadequate perfusion of maternal side of placenta as in maternal a placental diseases and abnormal uterine contractions as well as impaired maternal oxygenation in case of anemia. (**Gomella et al., ٢٠٠٤).**

Adrenaline is a hormone and a neurotransmitter. It's synthesized in neurons of the adrenal medulla and stored in the chromaffin granula; tow enzymes are responsible for adrenaline degradation: the Catecholamine-o-methyltransferase (COMT) and the monoamineoxydase (MAO). It's released by nervous stimulation in response to physical and mental stress affecting

Sympathetic nervous system. Their effects are like increasing heart rate and bronchodilatation. **(Oellien; ١٩٩٩)**

Few studies were done about the effect of HIE on adrenal gland. **Mialksoo et al., ١٩٨٨** found that the full-term newborn responds to asphyxia with graded catecholamine release. The epinephrine concentration in newborns with moderate HIE is lower than in newborns with mild HIE, which may reflect decreased sympathetic-adrenal function due to prolonged asphyxia.

Gorbachev et al; ١٩٧٦, made a study on urinary catecholamine excretion in ١٠٢ newborn boys on the ١st-٨th day after birth. It was shown that at the time of birth the noradrenaline level prevailed over the adrenaline level, but as soon as the ٣rd-٥th day the noradrenaline content displayed a relative reduction in both groups.

Aim of the work

The main objectives of this study are to:

١- Evaluate catecholamines level in the urine of newborn babies subjected to asphyxia.

٢- Investigate a possible association between the severity of hypoxic ischemic encephalopathy and the degree of adrenal gland affection.

Perinatal asphyxia & Hypoxic ischemic encephalopathy

Definition:

Perinatal asphyxia is an insult to the fetus or newborn due to lack of oxygen (hypoxia) and/or lack of perfusion (ischemia) to various organs. It is associated with tissue lactic acidosis. If accompanied by hypoventilation, it also may be associated with hypercapnia **(Aurora and Snyder, ٢٠٠٤).**

Hypoxic-ischemic encephalopathy (HIE) implies the interruption of supply of vital nutrients to the brain, mainly oxygen and glucose, sufficiently substantial to cause irreversible damage. **(Korthals and Colon, ٢٠٠٥).**

HIE is the hypoxic ischaemic brain injury as a result of perinatal asphyxia. Although HIE is not the most frequent complication of hypoxia ischaemia, but it is the most important consequence of perinatal asphyxia and it is one of the serious neurological problems of the perinatal period. Also HIE is the single most important perinatal cause of neurological morbidity in both full-term and premature infants **(Volpe, ٢٠٠١).**

There is no single tool that can yield a precise definion of perinatal asphyxia but the American Academy of pediatrics(AAP) and the American college of obstetrics and Gynecologists (ACOG)

committees of maternal fetal Medicine and fetus and Newborn in ١٩٩٦ defined certain criteria that must be present to confirm the occurrence of perinatal asphyxia. In cases in which such evidence is lacking, it can not be concluded that perinatal asphyxia exists **(AAP and ACOG, ١٩٩٦)**.

Table (١): Essential criteria of perinatal asphyxia:

١).Profound metabolic or mixed acedemia (pH<٧٫٠٠) on an umbilical cord arterial blood sample.
٢).Persistence of an Apgar score of ٠ to ٣>٥ minutes.
٣).Clinical neurologic sequelae in the neonatal period (e.g., seizures, hypotonia, coma or HIE).
٤).Evidence of multiorgan system dysfunction in the immediate neonatal period.

(AAP and ACOG, ١٩٩٦)

Incidence:

The risk for perinatal asphyxia is present in every pregnancy. However, consensus on the incidence of perinatal asphyxia has been difficult because of the non uniform clinical criteria on which different institutions based definition (**Thompson, ١٩٩٤).**

The incidence of perinatal asphyxia is about ١٫٠-١٫٥٪ in most centers and is usually related to gestational age and birth weight **(Aurora and Snyder, ٢٠٠٤).**

Etiology and risk factors:

Placental insufficiency is responsible for ٩٠٪ of asphyxial insults that occur in the antepartum / intrapartum periods as a result of inability to provide O٢ and remove CO٢ and H+ from the fetus. The remainder is postpartum, usually secondary to pulmonary, cardiovascular or neurological insufficiency **(Aurora and Snyder, ٢٠٠٤).**

Perinatal asphyxia could be exacerbated by any of the following conditions: impairment of maternal oxygenation, decrease of blood flow from mother to placenta or from placenta to fetus, impairment of gas exchange across placenta or in the fetal tissue and increase in fetal oxygen requirements **(Aurora and Snyder, ٢٠٠٤).**

These conditions may be **classified into:**

١. **Intrauterine conditions:**

Neonatal asphyxia may have its origin in utero, and is characterized by inadequate oxygenation and inadequate CO٢ elimination therefore; the lower respiratory centers are paralysed **(EL-Sherbini, ١٩٧٩)** as in:

- Inadequate oxygenation of maternal blood as a result of cardiac failure or pulmonary disease.
- Low maternal blood pressure in hypotensive mothers or due to compression of inferior vena cava and descending aorta by gravid uterus.
- Maternal hypertension and toxemia of pregnancy.