CRANIAL ULTRASOUND AND SERUM AMYLOID A AS A PREDICTORS OF OUTCOME IN TERM NEWBORN WITH HYPOXIC-ISCHEMIC ENCEPHALOPATHY

Thesis
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The Medical Doctorate Degree in Pediatrics

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Cranial ultrasound and serum amyloid A as a predictors of outcome in term newborn with hypoxic-ischemic encephalopathy

**Rational and background:**

Hypoxic ischemic encephalopathy is a major cause of neonatal death and brain injury. Of all neonates, even in developed countries, 2-5:1000 have brain injuries due to perinatal hypoxia *(Polat et al., 2012)*.

The American Academy of Pediatrics and the American College of Obstetricians and Gynecologists have defined neonatal hypoxic-ischemic encephalopathy (HIE) as an encephalopathy associated with hypoxia that occurs in the intrapartum period with no evidence of other anomalies. Essential criteria to be met: PH < 7 and base deficit $\geq$ 12 mmol/L in fetal/neonatal umbilical arterial blood obtained at the time of delivery *(Verklan, 2009)*.

There is a 10% risk of death in neonates who develop a moderate encephalopathy and a 30% risk of neuro developmental sequelae in those who survive. A severe encephalopathy is associated with a 60% risk of death and virtually guaranteed disabilities in survivors *(Shankaran et al., 2005)*.

Approximately 20% of neonatal HIE is primarily related to antepartum events as hypotension, placental vasculopathy, and insulin-dependent diabetes mellitus. Intrapartum events such as prolapsed cord, abruption placenta, and traumatic delivery have been linked to 35% of HIE cases. Conditions in the neonatal period may be responsible for 10% of HIE cases. These include congenital heart disease, severe pulmonary disease, severe recurrent apnea, and cardiac failure secondary to a large patent ductus arteriosus *(Volpe, 2008)*.

Pattern of injury occurs in 2 phases. The first phase is a primary energy failure related to the insult, and then a second energy failure occurs some hours later. The combined effects of cellular energy failure, acidosis, glutamate release, intracellular accumulation of calcium, lipid peroxidation, and nitric oxide neurotoxicity destroy essential components of the cell *(Verklan, 2009)*.

The clinical presentation depends on the severity, timing, and duration of the insult, with symptoms typically evolving over approximately 72 hours *(Volpe, 2008)*.

Encephalopathy was graded as mild, moderate and severe using the Sarnat and Sarnat system. The diagnosis is made through a careful history to note the presence of maternal factors that may have resulted in uteroplacental insufficiency antenatally *(Sarnat, 1976)*.
Diagnostic tests should rule out liver, renal, or cardiopulmonary dysfunction in addition to the usual complete blood cell count with differential and blood chemistry panels. Given the clinical condition of the neonate, it is important to monitor for hypoglycemia, hypocalcemia, hyponatremia, hypoxia, and acidosis (Verklan, 2009).

Ultrasound is very good at evaluating the extent of periventricular leukomalacia, as well as locating hemorrhagic complications (Ancel et al., 2006). Computed tomography is very helpful in identifying focal and multifocal ischemic brain injuries several weeks after the insult (Volpe, 2008). Magnetic resonance imaging is able to document brain injury patterns and may be predictive of the severity of the neurodevelopmental outcome (Liauw et al., 2007).

Supportive strategies include adequate perfusion, ventilation, and oxygenation. Prevention of hypoxemia is essential to prevent additional neuronal and white matter injury. On the other hand, hyperoxia also must be avoided as it is thought that it may result in decreased cerebral blood flow and further any injury (klinger. et al., 2005).
Hypothesis:

Serum amyloid A (SAA) is an acute phase inflammatory marker that is closely associated with ischemic injuries. Its expression in neonatal hypoxic ischemic encephalopathy (HIE) is increased. The concentration of serum amyloid A (SAA) correlates with the severity of encephalopathy and is associated with mortality (Aly et al., 2010).

Serum amyloid A (SAA) has been suggested to have a role in the pathogenesis of inflammation and its reduction can potentially be helpful in the treatment of ischemic disease. Patients with chronically increased SAA are considered at risk to develop vascular accidents. Serum amyloid A (SAA) correlates accurately not only with acute inflammation but also with intensity and degree of tissue damage and with cell necrosis (Hua et al., 2009).

Cranial ultrasound scanning with Doppler studies is a convenient and safe bedside measurement of cerebral hemodynamics. It predicts poor outcome of term infants with moderate or severe newborn encephalopathy (Jongeling et al., 2002).

Cranial ultrasound scanning in full-term infants with hypoxic–ischemic encephalopathy helps to time the onset of lesions, that is, whether the injury was inflicted antenatally, perinatally, or after birth. In addition, the evolution of lesions can be monitored and cranial ultrasound scanning can assist in distinguishing hypoxic–ischemic injury from other causes of neonatal encephalopathy, such as metabolic disease. Finally, cranial ultrasound scanning contributes to outcome prediction (van et al., 2009).
**Main goal:**

Assess the prognostic value of SAA and cranial ultrasound in term newborn with HIE.

**Specific Objectives:**

1- Study the relation of both SAA and cranial ultrasound with clinical grades of encephalopathy among term newborn suffered from HIE.

2- Examine the relation of SAA and cranial ultrasound with final outcome at discharge in term newborn with HIE.

**Subjects and methods:**

- **Study design**

  This study is a prospective cohort study.

- **Study sample**

  Thirty three newborns diagnosed as hypoxic-ischemic encephalopathy at birth and admitted at Neonatal intensive care unit (NICU) of Fayoum university hospital will be enrolled in present study.

  The inclusion criteria were established as follows: (1) Apgar score <5 at 5 min; (2) metabolic acidosis, (in fetal umbilical cord blood or in neonatal blood samples obtained on the first day of life); (3) delayed onset of respiration; (4) fetal distress (such as abnormal fetal heart rate and meconium stained amniotic fluid); (5) need for assisted ventilation (mask/balloon or intubation); (6) encephalopathy (lethargy/stupor, hypotonia and abnormal reflexes including an absent or weak suck); (7) presence of convulsions in the first 24 h of life; and (8) multiple organ dysfunction (encephalopathy and the involvement of at least one organ). Patients fulfilling at least two of the clinical findings were enrolled.

  Infants were excluded from the study if they met any of the following conditions: (a) conditions known to increase SAA such as sepsis or localized infection, (b) major congenital anomalies, (c) inborn errors of metabolism and (d) preterm births before 36 completed weeks.

  Full maternal and prenatal history was obtained for all cases. Full neurological examination was assessed during the first 24 hour of life including level of consciousness (alert, lethargy, or coma), muscle tone, tendon and complex reflexes, seizures and autonomic functions.
Assays for SAA were done in the first 24 hour of age and repeated at the seventh postnatal day.

Cranial ultrasound examinations were done at 48 hour and repeated at the seventh postnatal day.

Sepsis will be excluded depending on clinical and laboratory study.

**Data Analysis:**

Collected data will be presented as parameters, tables and graphs. The appropriate statistical methods of association and difference will be used after computerization using Statistical Package for Social Science (SPSS).

**Ethical considerations:**

This study will be submitted before the start of the fieldwork to Ethical review by an Independent Ethical Committee for ethical clearance.
References:


الموجات فوق الصوتية على المخ والبروتين النشوني كمؤشر على نتيجة مرض الاختناق الولادي في حديثي الولادة كامل النمو

يعتبر الاختناق الولادي من الأسباب الرئيسية لحدوث الوفيات في الأطفال، وتتراوح معدلات الوفيات من 10% في الحالات المتوسطة إلى 60% في الحالات الشديدة من المرض.

أسباب الاختناق الولادي يتمثل في أسباب متعلقة بالأم، مثل انخفاض ضغط الدم وأمراض المشيمة، وأسباب متعلقة بالولادة مثل الولادة المتعثرة وبعضها يتعلق بالطفل مثل العيوب الخلقية بالقلب.

الأعراض المرضية تظهر في الساعات الأولى بعد الولادة وقَد قام العالم سارنات بتقسيم المرض إلى ثلاث درجات الأولى بسيطة والثانية متوسطة والثالثة حادة طبقاً لحدة الأعراض.

يتم تشخيص المرض بالتأريخ المرضي للأم والطفل و باستخدام الاشعاع التشخيصي والخصائص التي تم تحديدها من قبل الأكاديمية الأمريكية لأطباء الأطفال وأطباء النساء والتوليد.

يتم علاج المرض بالحفاظ على العلامات الحيوية للطفل وعلاج الأعراض المصاحبة.

يترادد البروتين النشوني في حالات الاختناق الولادي ويتمكن استخدامه كمؤشر مع الحفاظ عليه. الموجات فوق الصوتية على الجمجمة كمؤشر على نتيجة المرض في الأطفال حديثي الولادة واحتمالية
الموجات فوق الصوتية على المخ والبروتين النشوي كمؤشر
على نتيجة مرض الاختناق الوليد في حديثي الولادة كاملي النمو

ماجستير طب الأطفال وحديثي الولادة

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