Case Report:

Evaluation of hypoxic-ischemic events in preterm neonates using trans cranial ultrasound

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Date of submission: 05 June 2014 ; Date of publication : 22 October 2014

Abstract:

Background: Hypoxic ischemic injury is an important cause of permanent damage to Central Nervous System that may result in neonatal death or manifest as cerebral palsy. 15-20% of preterm infants with hypoxic ischemic injury die in the neonatal period and 25-30% of survivors are left with permanent neurological developmental abnormalities (cerebral palsy, mental retardation). Trans-cranial ultrasound is performed and most readily available tool to assess the neonatal brain. It is safe and reliable technique for demonstrating the most frequently occurring forms of cerebral injury in preterm newborn, assessing the evolution of the lesion, and following brain development. The present study was planned to assess the predictive value of trans cranial ultrasonography imaging in evaluation of preterm neonates with hypoxic-ischemic brain injury and compare it with clinical findings.

Material and methods: Trans-cranial ultrasound was performed on 62 neonates of both sex born at gestational age less than 35 weeks with high frequency linear and curvilinear probe of 8.2 – 11 MHz.

Results: 35 males (56%) preterm neonates and 27 females (44%) preterm neonates were studied. All preterm neonates were less than 35 weeks of gestation by maternal dates. The maternal age was from 17 years to 40 years. They were 31(50%) primigravida of total. The most common obstetric risk factors observed were pre-eclampsia and eclampsia(25.8%), spontaneous preterm delivery (64.5%), IUGR(3.2%) and abruptio placentae(3.2%). In 1 (1.6%) preterm neonate out of 62, bilateral periventricular leukomalacia (PVL) was found, 6(9.6%) preterm neonates had grade I, 2(3.2%) preterm neonates had grade II and 1(1.6%) preterm neonates had grade III germinal matrix hemorrhage (GMH), 52 (83%) preterm the white matter was normal on ultrasound findings.

Conclusion: Trans cranial sonography is very good modality to find out hypoxic-ischemic events in preterm neonates. It helps in diagnosis of the abnormal neurological findings in clinically suspected preterm neonates. It was found to be most valuable predictor of outcome of hypoxic ischemic brain injury.

Keywords: Trans cranial sonography

Introduction:

Hypoxic ischemic brain injury in preterm neonates remains a serious condition causing significant mortality and long term morbidity. It is an important cause of permanent damage to CNS cells that may result in neonate's death or be manifested as cerebral palsy or mental deficiency. Hypoxia refers to arterial concentration of oxygen that is less than normal. Ischemia refers to blood flow to cells or organs that is insufficient to maintain their normal function.

Hypoxic-Ischemic Encephalopathy is an abnormal neurologic behavior in the neonatal period arising as a result of a hypoxic-ischemic event. 15-20% of
preterm infants with hypoxic ischemic injury die in the neonatal period and 25-30% of survivors are left with permanent neurological developmental abnormalities (cerebral palsy, mental retardation). 50-75% mortality rate is noted in severe hypoxic ischemic injury\(^2\).

In preterm neonates different types of hypoxic – ischemic brain injury can occur. Brain injury can be localized or diffuse. In localized brain injury arterial or venous peri-ventricular infarctions are encountered. Causes of arterial infarction are coagulopathies, vasculopathies, polycythemia and cyanotic congenital heart disease. Diffuse ischemic brain injury is the result of decreased brain perfusion or hypoxemia. This may results in ischemic injury in the form of white matter injury in preterm infants. In general, infants with signs of hypoxic-ischemic episodes show distress prior to delivery, have abnormal Apgar scores, require resuscitation at birth, and have neurological abnormalities within the first days of life, such as feeding difficulties, irritability, abnormality of tone, seizures, and decreased level of consciousness\(^3,4\).

Different imaging modalities are available to detect neonatal brain injury, including cranial ultrasonography, computer tomography (CT), and magnetic resonance imaging (MRI). Cranial ultrasonography can be performed at the bedside, which is an advantage in unstable and / or preterm newborn. It is suitable for screening and follow up examinations. It is generally performed using the anterior fontanelle as an acoustic window. The posterior fontanelle and mastoid can be used as acoustic window to study the posterior fossa and brain stem. The sensitivity and reliability of cranial ultrasonography for detection of germinal matrix haemorrhage, intraventricular haemorrhage, and periventricular Leukomalacia newborn is well-known\(^3,4,5,6\).

MR imaging has the advantage of superbly displaying soft tissue contrast differentiation and moreover displaying the exact extent and site of brain injury better than cranial ultrasonography. Tran cranial ultrasound (TCUS) is a safe and reliable technique for demonstrating the most frequently occurring forms of cerebral injury in preterm newborn, assessing the evolution of lesions, and following brain development\(^3,4,5\). In our study, we assessed the predictive value of cranial ultrasonography imaging for outcome and to compare with clinical findings in pre term neonates with hypoxic-ischemic brain injury.

**Materials and methods:**

62 preterm neonates of both sexes born at a gestational age less than 35 weeks were included in the study.

Transcranial ultrasonography were performed in all preterm infants, from the 3rd day of the birth. It is mainly performed through anterior fontanelle in both coronal and sagittal planes.

All three convex (3-5-5 MHz), cardiac (3.5-5MHz), and linear (7-11MHz) transducer were used.

The transducer frequency was set at 8.2 to 11 MHz for detection of cortical and / or sub cortical abnormalities, where as deeper structures were assessed with lower frequencies down to 5.0 MHz. Coronal images were obtained by placing the transducers transversely across the anterior fontanelle. Sagittal images were obtained by placing transducer longitudinally across the anterior fontanelle angling it to each side.
The midline is first identified through the interhemispheric fissure by the curving line of the corpus callosum. Shallow angulation of 10 degree will show the normal small lateral ventricles. The transducer was angled so that the anterior portion of the sector is directed more medially and the posterior sector more laterally so that the entire lateral ventricle is imaged in a single plane.

Results:

**TABLE 1: Relation of BOH with USG findings**

<table>
<thead>
<tr>
<th>Bad Obstetric history</th>
<th>No of preterm neonates</th>
<th>Percentage</th>
<th>USG findings (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spontaneous preterm delivery</td>
<td>40</td>
<td>64.5</td>
<td>GMH grade I (1)</td>
</tr>
<tr>
<td>Abruptio-placenta</td>
<td>2</td>
<td>3.2</td>
<td>GMH grade II(1)</td>
</tr>
<tr>
<td>Pre eclampsia</td>
<td>16</td>
<td>25.8</td>
<td>GMH grade I (4)</td>
</tr>
<tr>
<td>IUUGR</td>
<td>2</td>
<td>3.2</td>
<td>GMH grade III(1)</td>
</tr>
<tr>
<td>Maternal infection</td>
<td>2</td>
<td>3.2</td>
<td>Nil</td>
</tr>
</tbody>
</table>

**TABLE 2: Relation between clinical signs and USG findings**

<table>
<thead>
<tr>
<th>Clinical signs in preterm neonates</th>
<th>Weight in gms (mean)</th>
<th>Gestation age in week (mean)</th>
<th>OBGY history</th>
<th>USG findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absent Moro’s reflex</td>
<td>1766</td>
<td>32</td>
<td>Spontaneous preterm delivery (1)</td>
<td>GMH G I (1) Bilateral PVL (1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Pre eclampsia(3)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Maternal infections (1)</td>
<td></td>
</tr>
<tr>
<td>Unequal pupil size</td>
<td>1813</td>
<td>32.3</td>
<td>Spontaneous preterm delivery (6)</td>
<td>GMH G I (4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Pre eclampsia(5)</td>
<td></td>
</tr>
<tr>
<td>Absent Moro’s reflex and Unequal pupil size</td>
<td>1666</td>
<td>31</td>
<td>Abruptio-placenta(1)</td>
<td>GMH G II (2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Pre eclampsia(2)</td>
<td></td>
</tr>
</tbody>
</table>

**Discussion:**

Hypoxic ischemic brain injury is one of the major complications followed after perinatal asphyxia. It remains the major problem in developing countries where incidence may be high. The present study is directed towards early recognition of risk factors causing perinatal asphyxia and comparing clinical findings, evaluation role of cranial ultrasound in preterm neonates with hypoxic ischemic brain injury using early intervention to reduce the sequelae. Brown
and Purvis and Finer et al have taken the following factors into consideration: Ante partum disorder, fetal distress, abnormal Apgar score, need for immediate neonatal resuscitation and abnormal neurological examination in neonates.

Neurological lesions of the preterm brain comprise primarily of germinal matrix hemorrhage (GMH), periventricular leukomalacia (PVL) and post hemorrhagic hydrocephalus (PHH). Our study was conducted on 62 preterm neonates of both sexes born at a gestational age less than 35 weeks. In 1 (1.6%) preterm neonate out of 62, bilateral periventricular leukomalacia (PVL) was found. This was observed in a case of pre-eclampsia.

In 6 (9.6%) preterm neonates grade I GMH was observed. Preterm neonates born spontaneously vaginally was found in 40 (64.5%) and these infants were near to normal on USG findings. Only one out of these 40 neonates indicated GMH Grade I USG findings. Other grade I GMH were observed in pre-eclampsia and IUGR.

It was observed that 2 (3.2%) preterm neonates had grade II GMH amongst which along with pre-eclampsia there was a case of abruption placenta and 1 (1.6%) preterm neonates had grade III germinal matrix hemorrhage (GMH) which was observed in a case of IUGR.

52 (83%) preterm showed normal white matter on ultrasound findings.

It was observed that, preterm neonates delivered with history of eclampsia, pre-eclampsia and prolonged 2nd stage of labour had a high risk of mortality due to hypoxic ischemic brain injury complication.

Severity of outcome increases with severity of hemorrhage. Grade II GMH can result in major neurologic deficits in 15% of infant, while grade III GMH have a 35% incidence of neurologic sequelae. All grades of GMH have a worse prognosis for neurologic outcome if parenchymal echo densities are present on a head sonogram.

Grade IV GMH with large intraparenchymal echo densities historically have resulted in a 90% chance of major motor deficits and more than 50% incidence of cognitive impairment. Extensive white matter involvement and subsequent connectivity derangements in grey matter account for much of the increased morbidity of grade IV hemorrhage.

**Conclusion:**

Premature newborns are vulnerable to the hazards of extra-uterine life with fragile cerebral vasculature and ongoing neurogenesis and synaptogenesis. They are susceptible to even mild hypoxic-ischemic events, and yet the infant are frequently tough and tenacious with life.

Total number of admission for neonatal intensive care for a period of 12 months at our centre was approximately 350. 62 babies were diagnosed as pre term hypoxic ischemic brain injury in two year duration and cranial ultrasound was advised.

- 84% of preterm neonates were normal on cranial ultrasound. Remaining 16% detected with preterm hypoxic ischemic brain injury.
- Pre eclampsia, eclampsia, spontaneous preterm birth of neonate, prolonged second stage of labour leading to asphyxia of babies were detected obstetric risk factors for hypoxic ischemic brain injury.

Abnormal neurological findings at the time of birth and or till the time of discharge were found...
most valuable predictor of outcome of hypoxic ischemic brain injury.

Total incidence of hypoxic ischemic brain injury in preterm neonates was 16% in our study.

Frequency of hypoxic ischemic brain injury was inversely proportional to age of gestation of preterm neonates and weight of neonates.

Study result shows that hypoxic ischemic brain injuries are seen more among preterm neonates who undergo more perinatal stress.

Our study results suggests that frequency of hypoxic ischemic brain injury in preterm neonates is more in relation to hypotonia, unequal pupil size and decreased or absent Moro’s reflex.

The most common location for injury to the premature brain is the germinal matrix, periventricular white matter. Because thalami, brain stem and cerebellum in the immature brain have high metabolic activity, they are more susceptible to injury in severe hypotension, and the insult manifests as increased echogenicity of the injured brain at US.

Source(s) of support:
The study was not supported by any grant or financial supporting agency.

Acknowledgement:
We are thankful to Dr. Amarjit Singh, Dean- Pad. Dr. D.Y. Patil Medical College, Hospital and Research Center, Pune for his valuable inspiration.

Conflicts of interest of each author/ contributor:
Authors/Contributors declare that none of them have any conflict of interest. Statement by Authors: This manuscript has been read and approved by all the authors. Authors believe that the manuscript represents honest work and each author takes responsibility for the integrity of the work as a whole from inception to the published article. This is joint efforts of each author with respect to intellectual content, literature search and manuscript preparation and review

1 : Grade I germinal matrix hemorrhage

2 : Grade II germinal matrix hemorrhage
3 : Grade III germinal matrix hemorrhage

4 : Bilateral periventricular leukomalacia

References: