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Original Research Article

Prognostic value of resistive index (measured in anterior cerebral artery) in term neonates with hypoxic ischemic encephalopathy

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ABSTRACT

Background: Perinatal asphyxia refers to a condition during the first and second stage of labor and soon after birth in which impaired gas exchange leads to acidosis, hypoxemia, and hypercarbia. The Doppler technique is a non-invasive method that can be used at the bed side without disturbing patients, for risk of subsequent neurodevelopment impairment in HIE. It has been proven that impaired cerebral circulation plays the main role in the pathogenesis of hypoxic ischemic brain injury in neonates.
Methods: Doppler sonography conducted in all enrolled subjects. Cerebral blood flow parameters-peak systolic velocity, end diastolic velocity and resistive index were measured in anterior cerebral artery bilaterally on parasagittal planes obtaining the images through the anterior fontanelle with in first 72 hours.
Results: In our study we found that death during hospital stay in neonates with normal RI and abnormal RI is 13% and 28.6% respectively ($p<0.01$). Abnormal neurological outcome of 70.6% at 6 months and 64.7% at 12 months in patients with abnormal RI and 23.3% at 6 months and 18.6% at 12 months in patients with normal RI ($p<0.01$).
Conclusions: There is a significant correlation between neurodevelopmental disabilities and cerebral blood flow parameters in neonates with hypoxic ischemic encephalopathy. Detection of increased or decreased in cerebral blood flow velocities in neonates with in first 72 hours postpartum has a significant prognostic value related to death and long-term neurodevelopmental outcome.

Keywords: Cerebral circulation, Resistive index, Neurodevelopment

INTRODUCTION

According to WHO classification of disease ICDS10, severe birth asphyxia is when APGAR score at 1 min of life is 0-3. Mild and moderate birth asphyxia is when APGAR score at 1 min is 4-7. Among neonates with hypoxic ischemic encephalopathy 15-20% die and nearly 25% develop permanent neurological deficits.[1,2] APGAR score, cord blood acidosis (Umbilical Artery ph <7.20) and neonatal acidosis (capillary blood ph<7.3) with in first hour of life have been used to predict long term outcome with limited usefulness.[3-6] More sensitive technique like neuroimaging are limited by cost and expertise.[7] The rapid advances in neonatal intensive care unit (NICU) have decreased the incidence of infants with adverse neurodevelopment outcomes; however, birth asphyxia is the major cause of hypoxic-ischemic brain injury in neonates born at term.[8] According to recommendations of American academy of neurology and the practice committee of the child neurology society, the measurements of resistive index (RI) and end diastolic flow velocity (EDFV) in the anterior cerebral artery are performed in order to assess cerebral perfusion and early prediction of outcome.[9] An increase in EDFV indicates local or diffuse vasodilatation, caused by increased pCO2 in case of asphyxia and accumulation of metabolites.[10,11]

It has been proven that impaired cerebral circulation plays the main role in the pathogenesis of hypoxic ischemic brain injury in neonates. Studies from high income countries have found decreased cerebral resistive index to differentiate asphyxiated neonate from healthy control and to predict the risk of subsequent neurodevelopment impairment. Resistive index (RI) measured for all neonates within 72 hrs. of life using pulse wave Doppler ultrasound and Signals recorded from anterior cerebral artery in the sagittal plane. Resistive index calculated as:

$$RI = (S - D)/S$$

Where S is peak systolic velocity and D is ending diastolic velocity. RI between 0.56 to 0.80 is considered to be normal.[12,13] Loss of cerebral autoregulation in hypoxic ischemic encephalopathy (HIE) can predispose to reduced/absent diastolic flow in cerebral arteries leading to increased RI (>0.80) or elevated diastolic flow due to arterial vasodilation resulting in reduced RI (<0.56).

METHODS

This was a hospital-based Prospective observational study conducted in neonatal intensive care unit in Department of Pediatrics of Government Medical College Srinagar. The study duration was 24 months from November 2018 to November 2020. The aim of the study was to determine the role of blood flow parameters via color Doppler ultrasonography in postasphyxial full term neonates within 72 hrs. of life.

Inclusion criteria

Inclusion criteria were; Full term neonates i.e. >37 weeks born with perinatal asphyxia APGAR score <5 at 5 min of life, need for positive pressure ventilation for >1 min at birth and evidence of moderate to severe HIE based on Sarnat and Sarnat scale.

Exclusion criteria

Exclusion criteria were; Premature neonates, full-term neonates with congenital or chromosomal abnormalities and congenital brain infection, suspected metabolic disease and Neonates admitted beyond 72 hours birth or received hypothermic treatment.

Patients were called for neurodevelopmental assessment at six and twelve months. Neurodevelopmental assessment was done by developmental assessment scale for Indian infants (DAS-II) a modified version of Bayley Scale of infant development. Mortality and/or neurodevelopmental outcome was assessed at 6- and 12-months age. Death is defined as all causes of mortality occurring before 12 months of age or lost on follow up.

Data collection

All neonates fulfilling the inclusion and exclusion criteria were enrolled in the study. An informed consent was taken from the parents or guardians of the patients. The ethical clearance was provided by the hospital ethical committee board.

Statistical methods

The recorded data was compiled and entered in spread sheet (Microsoft Excel) and exported to data editor SPSS version 20.0 (SPSS Inc, Chicago, USA) categorical variables were summarized as frequencies and percentages. Chi-square test or Fisher's exact test which ever appropriate was applied for comparison of categorical variables. Relative risk along with 95% CI was also reported, $p<0.05$ was considered to be significant.

RESULTS

A total of 110 neonates were enrolled in the study with HIE. They were classified according to Sarnat clinical staging grade II and grade III. The mean gestational age was 38.1 weeks in patients with normal RI and 37.9 weeks with abnormal RI patients. The mean birth weight was 2.79 kgs in patients with normal RI and 2.83kgs in patients with abnormal RI patients. 79.6% patients were delivered via normal vaginal delivery and 20.4% via lower segment caesarean section with normal RI and 66.1% and 33.9% patients with abnormal RI were delivered via normal vaginal delivery and lower segment caesarean section respectively. Based on color Doppler finding, neonates were classified as neonates with normal resistive index (RI=0.56-0.8) N=54 and neonates with abnormal resistive index (RI <0.56 or >0.80) N=56. A total of 75.9% of patients with stage II and 24.1% of patients with stage III of HIE with normal RI and 69.6% of patients with stage II and 30.4% of patients with stage III stage of HIE with abnormal RI (Table 1). Among 110 neonates included in study during the study period 23 died during hospital stay 10 lost follow up. Presence of abnormal resistive index was associated with a significant higher risk of death and abnormal neurodevelopmental outcome at 6 and 12 months. In our study we found that death during hospital stay in neonates with normal RI and abnormal RI is 13% and 28.6% respectively ($p<0.01$). Abnormal neurological outcome of 70.6% at 6 months and 64.7% at 12 months in patients with abnormal RI and 23.3% at 6 months and 18.6% at 12 months in patients with normal RI ($p<0.01$). Abnormal neurosonogram is defined as increased periventricular echogenicity and hyper echogenicity of basal ganglia within 72 hours of life. 74.1% of patients developed seizures with normal RI and 96.4% of patients developed seizures with abnormal RI. 13% of patients died during hospital stay with normal RI and 28.6% of patients died during hospital with abnormal RI (Table 2).

Table 1: Demographic characteristics of enrolled population.

Baseline variable		Neonates with normal RI (N=54), Frequency (%)	Neonates with abnormal RI (N=56), Frequency (%)
Gestational age, (weeks) mean (SD)		38.1 (1.205)	37.9 (1.081)
Birth weight (kg) mean (SD)		2.79 (0.295)	2.83 (0.324)
Delivered via normal vaginal delivery		43 (79.6)	37 (66.1)
Stage of HIE (Sarnat Sarnat System)	**Stage II**	41 (75.9)	39 (69.9)
	Stage III	13 (24.1)	17 (30.4)

Table 2: Association of RI with morbidity in HIE.

Outcome variables	Normal resistive index (N=54), Frequency (%)	Abnormal resistive index (N=56), Frequency (%)	Relative risk (95% CI)	P value
Abnormal neurological at 6 months	10 (23.3)	24 (70.6)	3.7 (2.18-6.38)	<0.01
Abnormal neurological at 12 months	8 (18.6)	22 (64.7)	5.1 (2.53-10.45)	<0.01
Neonatal seizers	40 (74.1)	54 (96.4)	1.3 (1.10-1.54)	<0.01
Death during hospital stay	7 (13)	16 (28.6)	2.2 (0.98-4.93)	<0.05
Need for inotropes	26 (48.1)	36 (66.1)	1.4 (0.98-1.92)	0.057
Abnormal neurosonogram	9 (16.7)	36 (64.3)	3.9 (2.06-7.23)	<0.01

DISCUSSION

In our study we used color Doppler ultrasound to detect the pattern of blood flow velocities in anterior cerebral arteries, as color Doppler ultrasound is a non-invasive method which allows repeated and safe assessment of hemodynamics in neonatal units.[14] In this prospective study 110 cases eligible for study were observed with HIE. 54 cases with resistive index between (0.56-0.80) and 56 cases resistive index either <0.56 or >0.80. Among 110 cases 23 died during hospital stay and 10 lost follow-up, 77 cases were followed at 6 and 12 months. Neurodevelopmental assessments were done at 6 and12 months, these cases were evaluated for motor and mental deviation quotient as per DASII scale. Our study is consistent with the study conducted by Kudreviciene et al.[15] they analyzed the relationship of cerebral blood circulation parameters peak systolic flow velocity, end diastolic flow velocity and RI at 12-24 h after birth. They analyzed that having a lower RI value is associated with severe impairment of motor and mental development at12 months of age. Kirimi et al investigated the relationship of blood flow parameters registered during the first 12 h after birth, they found that neonates whose peak systolic flow velocity and end diastolic flow velocity of cerebral blood flow were significantly lower, and RI was significantly higher, were found to have cerebral palsy (CP) and impairment of the mental and neuromotor development at 12 months of age.[16] In our study 74.1% of patients developed seizures with normal RI and 96.4% of patients developed seizures with abnormal RI. Similar results were obtained by Kumar et al.[17] A number of researchers analyzed associations between blood flow parameters measured via color Doppler ultrasound on the first few days of life and long-term outcomes.[9,12,18-20]

CONCLUSION

There is a significant correlation between neuro-developmental disabilities and cerebral blood flow parameters in neonates with hypoxic ischemic encephalopathy. Detection of increased or decreased in cerebral blood flow velocities in neonates with in first 72 hours postpartum has a significant prognostic value related to death and long-term neurodevelopmental outcome. After obtaining the results of various study on resistive index, the prognostic potential of resistive index is well established and need more studies. It is desirable that neonatologist get familiar with the optimal use of this imaging modality, especially in setting lacking sophisticated neuroimaging technique, so that neonatologist can use neuroprotective strategies especially therapeutic hypothermia.

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