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Original Research Article

Role of cerebral artery Doppler velocimetry in neonatal hypoxic ischemic encephalopathy

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ABSTRACT

Background: Hypoxic ischemic encephalopathy (HIE) is a brain injury that prevents adequate blood flow to the infant's brain. As compared to MRI and CT scan, neurosonogram is easily available, cost effective and easily reproducible, and is not associated with any radiation exposure or sedation. Therefore, the present study was conducted to assess the role of neurosonogram changes in grey scale and Doppler findings in evaluation of HIE.
Methods: It was a hospital-based case control study conducted over a period of one year in which 35 full term neonates born after 37 weeks of gestation with birth weight more than 2.5 kg and clinical evidence of HIE based on Sarnat and Sarnat classification were selected as cases. The 35 neonates other than HIE were matched by age and sex with the cases within 72 hours of birth were labelled as control.
Results: On doppler USG both resistive index (RI) and pulsatilitiy index (PI) in anterior cerebral artery (ACA) as well as middle cerebral artery (MCA) were significantly lower in HIE subjects compare to control group while peak systolic velocity (PSV) and end diastolic velocity (EDV) were significantly higher in HIE subjects. There was significant association of RI, PI and EDV with severity of HIE.
Conclusions: Spectral doppler imaging has very high sensitivity and specificity in diagnosis as well as grading of HIE. Therefore, it is recommended that in all neonates with clinical suspicion of HIE, neurosonogram along with spectral doppler of cranial arteries should be done for evaluation of HIE.

Keywords: HIE, Neurosonogram, RI, PI

INTRODUCTION

HIE is a brain injury that prevents adequate blood flow to the infant's brain.[1] It is a serious birth complication affecting both full term and preterm infants. It occurs in 1 to 3 per 1000 live births in developed countries.[2]

The pathogenesis of HIE after perinatal asphyxia in term infants lies in fetal hypoxia caused by various disorders in mother including inadequate oxygenation of maternal blood from hypoventilation during anaesthesia, cyanotic heart disease, respiratory failure or carbon monoxide poisoning.[3]

Various imaging modalities to evaluate HIE are neurosonogram, CT scan and MRI. Neurosonogram is the initial preferred imaging modality in evaluation of HIE. Ultrasound is a quick and easy tool and can be done bedside and can be used to assess the patient during an acute clinical deterioration, allowing the practitioner to implement appropriate therapies more rapidly. The use of multiple acoustic windows and variable frequency ultrasound transducers has improved its diagnostic sensitivity and specificity. With optimal technique and view, USG can delineate multiple focal intracranial pathologies as intracranial haemorrhages', calcifications, ischemia, and brain abscess. It can therefore, help in ruling out HIE mimickers.

Hypoxia can be assessed by ultrasound in which HIE can be detected by various findings on neurosonogram. In the acute phase we can see cerebral edema which takes time to develop and can be very mild in the early stages. USG findings can be negative for 24-48 hours following the insult. The only grey scale finding is white matter oedema which is demonstrated on USG by enhanced grey-white matter differentiation.[2] The echogenicity of the white matter increases in relation to the less echogenic, more compact cortical gray matter. Various other findings seen on grey scale are periventricular leukomalacia, germinal matrix hemorrhage and hydrocephalus. On spectral Doppler, various parameters assessed in cranial vessels are RI, PI, PSV, EDV. These values are altered due to alteration in the cerebrovascular hemodynamics as a result of hypoxia. There is decreased RI values less than 0.60 with significant edema.[2]

CT scan are helpful in identifying hemorrhagic lesions, diffuse cortical injury and damage to basal ganglia, however CT scan has limited ability to detect cortical injury during the first few days of life and is associated with exposure to radiation. Diffusion weighted MRI has high sensitivity and specificity early in the process and its ability to outline the topography of the lesion and changes occurring in thalamus and basal ganglia.[4] But MRI has limitation of being a time-consuming investigation, need of sedation and high cost. As compared to MRI and CT scan, neurosonogram is easily available, cost effective and easily reproducible, can be assessed in neonatal intensive care units, is less time-consuming procedure and is not associated with any radiation exposure or sedation.[5] Therefore, present study was conducted to assess role of neurosonogram changes in grey scale and Doppler findings in evaluation of HIE.

METHODS

Study design, settings and participants

It was a hospital-based case control study conducted over a period of one year from July 2019 to June 2020 in department of radiodiagnosis of Indira Gandhi medical college and hospital in Himachal Pradesh, India. 35 full term neonates born after 37 weeks of gestation with birth weight more than 2.5 kg with birth asphyxia and clinical evidence of mild, moderate and severe HIE based on Sarnat and Sarnat classification were selected as cases. Neonates with major congenital anomalies leading to hypoxia viz cardiac/pulmonary/neurological or ABO incompatibility were excluded from the study. Neurosonogram of all the neonates who came to the department of radiodiagnosis for indication other than HIE were matched by age and sex with the cases within 72 hours of birth were labelled as control.

Data collection

The caregivers of the study subjects attending the radiodiagnosis department were interviewed after taking informed written consent. Detailed birth history of patient was taken. Neurological examination was performed to evaluate for any neurological deficit, then the patient was subjected to neurosonogram including cerebral artery doppler examination within 72 hours of birth.

Sonographic procedure

After baseline investigations, all the patients were subjected to cranial ultrasonography and first of all on grey scale to look for any bleed or leucomalacia along with colour doppler of B/L anterior and middle cerebral arteries. The cranial sonography was performed using 5 MHz (convex) and 7.5 MHz (linear) transducer. All the cases were scanned in three planes. On sagittal scanning the centre of the transducer was placed over the anterior fontanel with the scanning plane aligned with the long axis of the head. Transducer was angled first to right and then to left. For coronal scanning transducer was rotated 90 degrees so that the scan plane aligned transversely and beam was angled forward and then backward. For axial scanning transducer was centred just above ear and beam angled towards the vault and down towards base of skull. It was then repeated on the other side. Colour doppler of ACA done by placing the probe on anterior fontanelle and MCA done through temporal fontanelle. Various doppler parameters that noted were-PI, RI, PSV, EDV.

Statistical analysis

Data were analyzed and statistically evaluated using SPSS software, version 25 (Chicago II, USA). Normal distribution of different parameters was tested by the Shapiro-Wilk normality test. Quantitative data was expressed in mean±standard deviation and depends on normality difference between mean of two groups were compared by student t test or Mann Whiney U test while for more than two groups ANNOVA test or Kruskal Wallis H test was used. Qualitative data were expressed in percentage and statistical differences between the proportions were tested by Fisher's exact test. P value less than 0.05 was considered statistically significant.

Ethical issues

All participants were explained about the purpose of the study. Confidentiality was assured to them along with informed written consent. The study was approved by the institutional ethical committee.

RESULTS

The age of patients in study group ranged from 1 day to 3 days with mean age of 2 days and the age of patients in control group ranged from 1 day to 3 days with mean age of 2 days. Table 1 shows demographic profile of both groups. Both the groups were comparable in term of gender distribution, birth weight and gestational age (Table 1). Out of 35 patients of study group, 22 (62.9%)

were HIE grade I, 3 (8.6%) were HIE grade II and 10 (28.6%) were HIE grade III.

Table 1: Demographic profile of study subjects.

Variables	Group		P value
	Study	Control	
Male:Female	22:13	22:13	-
Gestational age (weeks)	38.34±0.83	39.09±1.17	0.67
Birth weight (kgs)	2.90±0.22	2.90±0.28	0.84

The grey scale showed cerebral oedema in 2 patients of HIE III and ventriculomegaly in patient of HIE grade III which is indirect sign of intraventricular hemorrhage. Rest all patients were having normal findings on grey scale (Figure 1). On doppler USG both RI and PI in ACA as well as MCA were significantly lower in HIE subjects compare to control group while PSV and EDV were significantly higher in HIE subjects (Table 2). There was significant association of RI, PI and EDV with severity of HIE (Table 3).

Table 2: Comparison of doppler parameters between study group and control group.

Doppler parameters	Group		P value
	Study	Control	
RI			
ACA	0.67±0.14	0.74±0.04	0.01
MCA	0.68±0.14	0.76±0.04	0.002
PI			
ACA	1.33±0.36	1.58±0.32	<0.01
MCA	1.43±0.49	1.89±0.57	<0.01
PSV (cm/s)			
ACA	36.69±11.97	28.48±5.70	<0.001
MCA	41.95±12.73	31.47±6.47	<0.001
EDV (cm/s)			
ACA	11.58±5.34	7.65±1.92	<0.001
MCA	15.62±7.72	7.88±2.02	<0.001

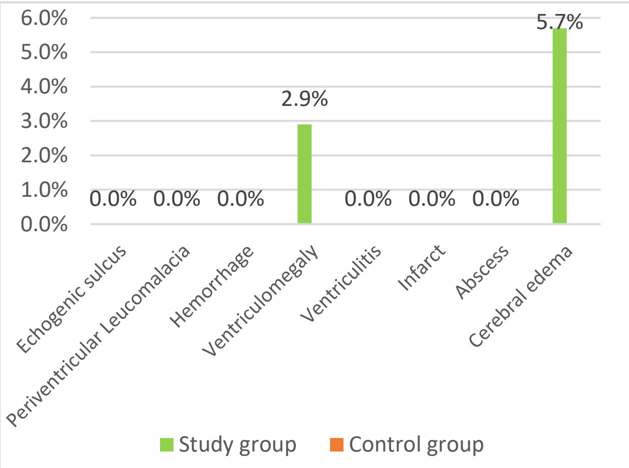

Figure 1: Distribution of patients according to grey scale findings.

Table 3: Association of doppler parameter with severity of HIE.

Variables	HIE grade			P value
	HIE grade I	HIE grade II	HIE grade III	
RI				
ACA	0.76±0.10	0.65±0.05	0.49±0.11	<0.001
MCA	0.77±0.09	0.59±0.04	0.52±0.13	<0.001
PI				
Right ACA	1.45±0.31	1.45±0.46	0.96±0.51	<0.001
Right MCA	1.65±0.46	0.98±0.17	1.05±0.51	0.01
PSV (cm/s)				
ACA	32.82±12.26	51.34±17.19	40.61±14.18	0.16
MCA	38.45±10.88	44.81±19.15	48.73±18.27	0.28
EDV (cm/s)				
ACA	8.4±4.31	19.4±2.4	16±5.5	<0.001
MCA	11.3±4.62	24.4±3.01	22.3±8.19	<0.001

DISCUSSION

Early diagnosis of cerebral hypoxia is of utmost importance to initiate early treatment to avoid its complications which are cerebral palsy, mental retardation, learning disabilities and epilepsy.[6]

In our study, on grey scale neurosonogram, only 2 neonates of HIE III were having cerebral oedema and one patient of HIE III had ventriculomegaly. Grey scale neurosonogram were normal in the remaining, however, spectral doppler of cranial vessels showed significant changes in doppler indices.

The alteration in Doppler indices is due to neonatal reaction to chronic as well as acute hypoxia which results in centralisation of blood flow to vital organs such as brain, heart and adrenal glands in order to maintain oxygenation as the autoregulatory mechanism results in secretion of vasodilators in cerebral vascular bed leading to vasodilatation and increase in blood flow in the cerebrovascular circulation. Therefore, resistance decreases resulting in decrease in RI and PI and increase in cerebral blood velocity and EDV.

Amongst all Doppler indices in the setting of HIE, RI has highly predictive of poor prognosis.[2] The resistance is the first factor to change in the setting of HIE. In the present study group, the mean RI in B/L ACA and MCA at 72 hours of birth was 0.76±0.10 and 0.77±0.09 respectively in HIE grade I, 0.65±0.05 and 0.59±0.04 in HIE grade II and 0.49±0.11 and 0.52±0.13 in HIE grade III. Mean RI in B/L ACA was 0.74±0.04 and MCA was 0.76±0.04 at 72 hours of birth in the control group. There was no significant difference between RI of control group and HIE I but there was significant reduction in RI with the increasing severity of hypoxia in HIE II and III. Finding of our study were corroborated with study of Eken et al (<0.55 cm/s), Rao et al (<0.6 cm/s), Stark et al (0.23 to 0.59 cm/s) where mean RI in severe HIE cases was also significantly lesser in severe HIE patients.[7-9]

The other Doppler parameters that were studied for HIE were PI, PSV and EDV. The mean PI in B/L ACA and MCA at 72 hours of birth was 1.45±0.31 and 1.65±0.46 respectively in HIE grade I, 1.45±0.46 and 0.98±0.17 in HIE grade II, 0.96±0.51 and 1.05±0.51 in HIE grade III in the study group. The control group had mean PI in B/L ACA was 1.58±0.32 and in MCA it was 1.89±0.57 at 72 hours of birth. There was no significant difference in PI between control group and HIE I. However, there was statistically significant decrease in PI as the severity of HIE increased. In study by Daven et al mean PI in severe HIE was 0.63 and in study of Archer et al mean PI was <0.55 which is similar to our study.[10,11]

The mean PSV in B/L ACA and MCA at 72 hours of birth was 32.82±12.26 cm/s and 38.45±10.88 cm/s respectively in HIE grade I, 51.34±17.19 cm/s and 44.81±19.15 cm/s in HIE grade II and 40.61±14.18 cm/s and 48.73±18.27 cm/s in HIE grade III. The value of PSV in all the grades of HIE does not show significant change, however, there is significant increase as compared to the control group. In the control group, mean PSV in B/L ACA was 28.48±5.70 cm/s and in B/L MCA it was 31.47±6.47 cm/s at 72 hours of birth. Finding of our study were similar to study by Ilves et al in which mean PSV was 26.5 cm/s in severe HIE cases.[12]

Limitations

As our hospital was a tertiary care centre so more severe cases of HIE might be selected in the study compare to general population so finding cannot be generalized to all HIE population.

CONCLUSION

Based on the finding of present study it can be concluded that grey scale cranial sonography alone has very low sensitivity and specificity in picking up findings in neonates with HIE. Spectral doppler imaging along with various doppler indices like RI, PI, EDV of bilateral anterior and middle cerebral arteries in HIE neonates has very high sensitivity and specificity in diagnosis as well as grading of HIE.

Recommendations

Based on the finding of our study, it is recommended that in all neonates with clinical suspicion of HIE, neurosonogram along with spectral doppler of cranial arteries should be done for evaluation of HIE.

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