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Prospective Study on the Importance of Colour Doppler Neuro Sonography in Assessing Short-Term Prognosis among Full-Term Neonates with Perinatal Asphyxia

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KEYWORDS
Perinatal asphyxia, End-diastolic flow velocity, Peak systolic flow velocity, Resistive index, Pulsatility index.

ABSTRACT:
The aim of the study was to determine the role of blood flow parameters evaluated by colour Doppler ultrasonography in neonates with birth asphyxia and correlate it with the short-term prognostic outcome - mortality. The present study which included 115 neonates confirms a role for cranial Doppler measurements like resistive index (RI), pulsatality index (PI), peak systolic blood flow velocity (PSFV) and end-diastolic blood flow velocity (EDFV), in conjunction with other clinical information, as a safe and cost-efficient method for prognostication of outcome in neonatal hypoxic-ischemic encephalopathy (HIE).

Introduction

Perinatal asphyxia is one of the main reasons for mortality and morbidity among newborns, with an estimated incidence of 1–8/1000 live births according to different studies.[1] The rapid advances in neonatal intensive care of late has reduced the incidence of poor prognosis of asphyxia like adverse neuro developmental outcomes. However, birth asphyxia is the important cause of hypoxic-ischemic brain injury in neonates born at term.[2] It is always a must to evaluate the severity of asphyxia to plan proper treatment and to prevent brain damage.[3] Computed tomography (CT) is generally of minimal help in this state due to numerous reasons.[4] MRI will be more useful but it cannot be used at the bedside. Colour Doppler is widely used nowadays which gives more information.[5,6] There are not much studies related to this modality. Thus, our study intends to discover the early diagnostic value of observing cerebral hemodynamic changes with Doppler ultrasound for neonatal HIE.

According to the recommendations of the American Academy of Neurology and the Practice Committee of the Child Neurology Society, the measurements of RI and EDFV in the anterior cerebral artery are done in order to evaluate cerebral perfusion and predict an outcome.[6] An increase in EDFV indicates local or diffuse vasodilatation, caused by increased pCO2 in case of asphyxia and accumulation of metabolites.[7,8] However, in many countries, colour Doppler ultrasonography is not widely applied in daily practice, and data on its diagnostic and prognostic potential remain scarce[8]. It has been proven through many studies that compromised cerebral blood flow has an important role in the pathogenesis of HIE in neonates. Yet, studies conducted so far have been insufficient to explain how changes in blood circulation parameters are related to short-term prognosis like mortality.

Methodology

Maternal history and other details were obtained from mothers' case sheet. After getting informed consent from the parents of the newborns delivered in the VMKVMC Hospital, Salem, India, who fulfil the inclusion and exclusion criteria, they were included in the study. Colour Doppler cranial ultrasound was performed at the bedside within the first 24 hours after birth while the newborn is awake and calm or when asleep. Measurements were done with a 2-5 MHz convex or phased array transducer of computed sonography system. The transducer was placed on the anterior fontanelle to detect hemodynamic parameters of bilateral anterior and middle cerebral arteries, including PSFV, EDFV, time-averaged mean flow velocity (TMFV), PI and RI. All the indices were measured over three complete cardiac cycles.

Statical analysis

Statistical analysis was done using SPSS Software version 21.0. The methods were used based on variables

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and outcomes. Mann Whitney score was used for non-parametric test and Student's t test to compare parameters of ultrasound.

Results

Mode of delivery	No. of patients	Percentage
Natural labour	58	51%
Lower segment Cesarian section (LSCS)	37	32%
Assisted vaginal delivery	20	17%

Table 1: Natural labour constituted about 51% in the study.

Course of labour	No. of patients	Percentage
Uneventful	95	83%
Prolonged first stage	1	1%
Prolonged second stage	14	12%
Obstructed	5	4%

Table 2: Course of labour was uneventful in 83%, prolonged first stage in 1%, prolonged second stage in 12% and obstructed labour in 4%.

Final diagnosis	No. of patients	Percentage
Birth asphyxia	63	55%
HIE of newborn	26	22%
Meningitis	1	1%
Neonatal aspiration of meconium	16	14%
Respiratory distress syndrome (RDS) of newborn	1	1%
Any other	8	7%

Table 3: In the study, 55% patients had birth asphyxia, hypoxic ischemic encephalopathy in 22%, Meconium aspiration syndrome in 14%, meningitis in 1%, RDS in 1%.

Cause of death	No. of patients	Percentage
HIE/moderate -severe birth asphyxia	17	95%
Meconium aspiration syndrome	1	5%

Table 4: Out of total 18 deaths, 95% were having HIE, 5% with meconium aspiration syndrome.

Ventilator required	No of patients	Percentage
Yes	16	14%
No	99	86%

Table 5: Ventilator support was required for only 16 patients.

Inotropes used	No. of patients	Percentage
Yes	18	16%
No	97	84%

Table 6: Inotropes were used only in 18 patients.

Cranial Doppler indices	Mean	Standard deviation
RI	0.62	0.12
PI	1.2	0.09
PSFV	24.31	3.2
EDFV	14.92	1.86

Table 7: Pulsatility index, resistive index, peak systolic flow velocity, end diastolic flow velocity were compared with the final outcome and discussed in detail.

Discussion

In our study, we selected around 115 patients and did a prospective observational study for a period of one year from January 2022 to January 2023. We included neonates who were full-term (≥37 weeks of gestation), neonates born with perinatal hypoxia or asphyxia requiring resuscitation, Apgar score at 5 minutes≤7 points, with foetal acidosis (umbilical artery blood pH < 7.2).

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We excluded patients who were pre-term (<37 weeks of gestation), neonates with congenital anomalies, chromosomal abnormalities, haemolytic disease of the new-born, and intra-cranial infection, severe sepsis with haemodynamic disturbances, or suspected metabolic diseases.

In our study, we started with analysing the age of the mother. Most of the mothers (76%) were of the age between 21-30 years which is the commonest reproductive age group. This was similar to a study done by Bongaartset, where the mean age was around 22.7 years.

Among mothers 23% were primi mothers. Second gravida were 59 per cent, while third gravida 18%. A study done by Kiyaniet et al. which dealt with these factors where most of the mothers were between 1-3 gravida, i.e., 64.80% (N=127) while 35.20 % (N=69) had ≥4 gravida, mean and standard deviation was 3.45 (+0.87). These results were similar to our study.

Similarly in our study group 27 patients had haemoglobin level less than 10 gm while the rest had more than 10 gm. Extensive literature review revealed that iron deficiency is a global nutritional problem affecting up to 52% of pregnant women. Throughout pregnancy, iron deficiency anaemia adversely affects the maternal and foetal wellbeing, and is linked to increased morbidity and foetal death. Adverse perinatal outcomes include intrauterine growth retardation, prematurity, and low birth weight, all with significant mortality risks. These were explained well in studies done by Abu et al.

In our study group, most of the neonates were delivered through normal vaginal delivery, among the 78 such deliveries, 20 were assisted vaginal deliveries with forceps or vaccum devices. The remaining were delivered by Cesarean section. These results were similar to a study done by Kiyani et al. where mode of delivery was spontaneous vertex delivery in 44.39%, Caesarean section in 32.14%, while 23.47% was instrumental delivery. Among these 115 mothers, spontaneous labour was common with 70% while the rest 30% had induced labour. Also, course of labour was uneventful in 83% of patients while the rest had prolonged or obstructed labour. These studies were similar to studies done by Babus et al.

Among total 115 babies in our study group 79 were male and the rest female. After delivery we weighed the babies in a standard weighing scale. Among 115 babies in our study, around 79% (N=91) were between 2-3 kg while only four babies were of low birth weight. In a study done by Kiyani et al. too mean weight of the newborns was calculated as 2621.37 (+74.21) grams

In our study group as a whole the mean age of mothers was 24.76, mean baby weight 2.76 kg, mean heart rate was143.6 beats per minute, mean respiratory rate was 61.73 per minute and mean duration of stay in hospital was 8.81 days.

Further we analysed Apgar score at one minute where 76% (N=88) had Apgar score between 4-7 and the rest had less than that, whereas after five minutes almost 96% of the patients had Apgar score between 4-7. Hence mean Apgar at one minute was 4.12 and at five minutes was 5.98. Similar results were seen in a study done by Bhagwani et al. Apgar score of <=3 at one minute was found in 58 babies (40%) and 87 babies (60%) had a score of 4-6 at one minute where all babies selected had Apgar score under 7.

Coming to heart rate most of the patients (77%) had heart rate between 120-160 per minute while about 11% of patients had heart rate less than 120 and 12% had heart rate more than 160. Respiratory rate was normal in 36 patients and was abnormal in 79 patients. Similar results on heart rate and respiratory rate were seen in studies done by Mcguireet Al.

When we evaluated the type of resuscitation required, tactile stimulation was enough in 73 babies while the rest needed one of the methods like bag and mask ventilation, chest compression and endotracheal intubation. Berglund et al. did a study on this which showed multiple methods of resuscitation similar to this study.

Coming to the duration of hospital stay, most of the babies were in the hospital for less tha10 days barring a few. This probably is a straight forward parameter where babies who are ill with asphyxia needs a longer stay for complete recovery and better prognosis.

Coming to final diagnosis, most common diagnosis was birth asphyxia followed by hypoxic ischemic encephalopathy of newborn. Meconium aspiration syndrome was seen in 16 cases while the rest had other causes which is similar to a study done by Endrichet Al. In our study 15 per cent of the babies died while the rest recovered and discharged. The cause of death in almost all cases was HIE with birth asphyxia. This is similar to the study done by Ekowochiet Al where the case fatality rate was 18%.
In our study, we classified the neonates according to Sarnat and Sarnat Staging for HIE. Most of the patients were in stage 1 (81%) while 17 babies were in stage 2 and five in stage 3. Outcome depended on staging where stage 2 and 3 had more mortality than stage 1 HIE

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babies. Similarly in our study, 16 babies required ventilator and 18 babies required inotropes during management.

We correlated the outcome among the babies with the cranial Doppler indices. Also, we correlated the need of inotropes, ventilator and Sarnat and Sarnat staging of HIE with the resistive index measured through cranial doppler. Among various parameters of cranial doppler we took four parameters for analysis. PI, RI, PSFV and EDFV with the final outcome i.e., death or alive, in both anterior cerebral artery and middle cerebral artery. To start with anterior cerebral artery, first we analysed resistive index which was inversely proportional to outcome. It had significantly higher values in neonates who died in comparison with neonates who were alive with a mean of 0.77 in died neonates and 0.59 in alive babies. Two of three studies examining RI values as a long-term predictors of outcome found worse outcomes among neonates with higher RI values as done by Estad et al.

Next, we analysed the PI which is also inversely proportional to the outcome. It had significantly higher values in neonates who died in comparison with neonates who were alive with a mean of 1.29 in died neonates and 1.19 in alive babies. Measurements using cranial doppler ultrasonography suggest that increased cerebral blood flow velocity and a low cerebral artery pulsatility index are present after asphyxia.

Further we analysed the PSFV and EDFV, both are directly proportional to the outcome. There were significantly lower values in neonates who died in comparison with neonates who were alive with a mean PSFV of 21.72 in died neonates and 24.79 in alive babies. Similarly in EDFV to mean was 11.67 in died neonates and 15.52 in alive neonates.

Similar evaluation was done in middle cerebral artery indices too. First, we analysed resistive index which was inversely proportional to outcome. There were significantly higher values in neonates who died in comparison with alive neonates with a mean of 0.8 in died neonates and 0.6 in alive babies.

Next, we analysed the pulsatility index which is also inversely proportional to the outcome. It had significantly higher values in neonates who died in comparison with neonates who were alive with a mean of 1.38 in died neonates and 1.21 in alive babies.

Further we analysed the PSFV and EDFV, both are directly proportional to the outcome. There were significantly lower values in neonates who died in comparison with alive neonates with a mean PSFV of 22.2 in died neonates and 25.17 in alive babies. Similarly in EDFV to mean was 12.15 in died neonates and 15.85 in alive neonates.

We further analysed the resistive index alone in both anterior and middle cerebral arteries and correlated with the HIE staging, ventilator requirement and inotrope usage. To start with staging of HIE, there was increase in the RI values with worsening of stage in both anterior cerebral artery and middle cerebral artery. Similar results were seen in ventilator requirement and inotrope usage in relation with RI wherein all factors increase in RI has a bad outcome – either morbidity or mortality.

These results of colour Doppler were done previously in studies done by Senthil et al. where loss of cerebral autoregulation in HIE can predispose to reduced/absent diastolic blood flow in cerebral arteries leading to increased RI (>0.80) or elevated diastolic flow due to arterial vasodilation resulting in reduced RI.[10,14] Decreased RI has been well documented in asphyxia and found to increase the risk of death or cerebral palsy by 23.4 times. There is increase in RI in early stages of asphyxia whereas it falls at later stages when the condition worsens and prognosis becomes worse as done in a study by Gerner et al. In general, RI values should generally stabilise into the normal range of 48 hours post-injury. Failure to do so more than 72 hours post-injury, which equates with the time period in which post-cooling RI values were obtained, may therefore suggest a more severe brain injury and subsequently worse motor outcome. Also, the study suggests that pre-cooling RI <0.60 may broadly differentiate neonates who are more likely to have outcomes of severe neuro developmental disability or death by the age of 20-32 months, hence abnormal RI levels has a bad prognosis. Similarly other values have a similar effect on the prognosis of the neonates.

Conclusion

In conclusion, the present study confirms a role for cranial Doppler measurements like RI, PI, PSFV and EDFV in conjunction with other clinical information as a safe and cost-efficient method for prognostication of outcome in neonatal HIE. Considering the prognostic potential of RI in neonates with HIE, it is desirable that neonatologists get familiar with the optimal usage of this imaging modality, especially in settings lacking sophisticated neuroimaging techniques. This study results also open the gates for further research with more specific end points to further confirm the importance of cranial Doppler and its factors as a tool to assess the severity and mortality.

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