Original Research Article

To evaluate the role of MRI of hypoxic ischemic encephalopathy

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Abstract

Background: Hypoxic ischemic encephalopathy (HIE) is one the common causes of neonatal fatality due to perinatal asphyxia. The long-term outcomes of HIE are impaired mental and motor development, hearing loss, recurrent seizures and cerebral palsy. MRI is increasingly becoming the gold standard in diagnosis of HIE as it involves no radiation and can be performed during a neonate physiological sleep. **Material and Methods** :This prospective study was conducted in a tertiary care hospital for a period of 1 year from March 2019 to February 2020. at Subbaiah Institute of Medical Sciences. A total of 60 patients with history of birth asphyxia were included in the study who underwent MRI of brain and were followed up clinically at the end of one year to assess the neurological outcome. MRI was done on Philips Achieva 1.5 Tesla MRI system. The neonate was sedated using pedichloryl syrup or intravenous Ketamine/Propofol before start of study was administered by the attending anaesthetist and was placed in the supine position. The section thickness was 3-4 millimeter. Only plain MRI studies were done without using intravenous contrast. **Result** :A total of 60 patients who fulfilled the selection criteria during the study were enrolled. In this study, the maximum number of patients were in the age group of <1 year which were 45% (n =27). Of the 60 babies, 37 were males and 23 females, which correspond to 61.6% of male and the rest female babies. Out of the 60 babies 39 were term babies, which corresponds to 65% and 35% of pre-terms. In our study, maximum patients, i.e., 51.6% (n = 31) were having Apgar score of 4-6 followed by ≤3 score were26.6% and least were > 7 score were 21.6%. In HIE 2 cases, 31.6% had involvement of corpus callosam. 23.3% had PVL, 21.6% had basal ganglia or thalamus lesion. There was no MRI evidence of HIE in 13.3%. Out of 6 babies with stage 3 HIE, 55% had involvement of bilateral basal ganglia. 30% had bilateral thalami lesion and the rest showed subcortical white matter lesion. **Conclusion** :MRI is useful in establishing the clinical diagnosis, assessing the severity of injury, and thereby prognosticating the outcome. Familiarity with imaging spectrum and insight into factors affecting the injury will enlighten the radiologist to provide an appropriate diagnosis.

Keywords: Hypoxic ischemic encephalopathy, MRI, Neurological impairment.

Introduction

Hypoxic-ischemic encephalopathy (HIE) in term and near-term newborns is an important cause of morbidity and mortality. [1] HIE is perinatal asphyxia and it long term outcomes are impaired mental and motor development, hearing loss, recurrent seizures and cerebral palsy.Therapeutic hypothermia has been a major advance in the management of neonatal HIE.

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Meta-analyses of several large multicenter trials have concluded that hypothermia treatment is associated with a reduction in death and neurological impairment in early childhood. [2] These results were confirmed in the recently reported Infant Cooling Evaluation (ICE) randomized controlled trial, in which whole-body hypothermia treatment was shown to reduce death or major sensorineural disability at 2 years of age compared with normothermia. [3]Magnetic resonance imaging (MRI) assists in defining the nature and extent of perinatal brain injury. Because hypoxic-ischemic (HI) cerebral injury is a dynamic process, the diagnostic and prognostic utility of MRI needs to be interpreted in the context of the timing of the MRI.

Patterns of brain injury on conventional T1- and T2-weighted MRI at 1 week after birth have been shown to predict abnormal neuromotor outcome in early childhood. [4] Diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC) changes with HI injury are most prominent from days 2 through 5 and can be detected earlier than abnormalities detected on the conventional T1- and T2-weighted MRI. [5] In the Total Body Hypothermia for Neonatal Encephalopathy (TOBY) trial, MRI studies performed a median of 8 days after birth reported a reduction in the incidence of cerebral injury compared with normothermia but consistent prognostic value from MRI irrespective of treatment. [6] However, we need to determine whether this prognostic utility is similar in a different cohort with MRI performed at a different median age.The patterns of brain injury on conventional T1- and T2-weighted MRI at one week after birth predict abnormal neuromotor outcome in early childhood. Diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC) changes with HI injury are most prominent from days two through five and can be detected earlier than abnormalities detected on the conventional T1- and T2-weighted MRI. [7] The aim of the study was to evaluate MRI findings in patients with HIE and in prognosticating neurological outcome.

Material and Methods

This prospective study was conducted in a tertiary care hospital, Subbaiah Institute of Medical Sciences for a period of 1 year from March 2019 to February 2020. A total of 60 patients with history of birth asphyxia were included in the study who underwent MRI of brain and were followed up clinically at the end of one year to assess the neurological outcome.

Inclusion criteria

Full term (>37 weeks of gestation),
Pre-term (<37 weeks of gestation)
Neonates born with birth asphyxia and APGAR score at 5 minutes after birth

Exclusion criteria

Term or preterm neonates with infection and suspected Metabolic disease.

Patients with prosthesis, heart valve prosthesis, artificial/prosthetic limb, surgical staples, clips or metallic sutures and claustrophobia.MRI was done on Philips Achieva 1.5 Tesla MRI system. The neonate was sedated using pedichloryl syrup or intravenous Ketamine/Propofol before start of study was administered by the attending anaesthetist and was placed in the supine position and the following protocol was followed.

- T1-weightedspin-echo (TR/ TE, 400/13-308),
- T2-FLAIR (TR/TE, 9500/120),
- Axial T2 FSE TR/TE (4000/102) Echo train length 24,
- DWI (TR/TE 8000/100.7)
- SWAN sequence.

The section thickness was 3-4 millimeter. Only plain MRI studies were done without using intravenous contrast.

Statistical analysis

Statistical analysis was done using SPSS version 15 and sensitivity, specificity, positive and negative predictive value of MRI in comparison to clinical follow up at the end of one year was assessed. A grading system was devised for both MRI and clinical follow up for statistical purpose.

Result

A total of 60 patients who fulfilled the selection criteria during the study were enrolled. The data were analysed, and the final observations were tabulated as below. In this study, the maximum number of patients were in the age group of <1 year which were 45% (n =27) of total followed by age group 2–12 months having 35% (n = 21) in this group and 20% were more than 1 year in table 1.

Table 1: Distribution of the number of children according to age group

Age group	No. of patients	Percentage
< 1 month	27	45
2-12 months	21	35
> 1 year	12	20
Total	60	100

Table 2: Distribution of Gender

Sex	No. of patients	Percentage
Male	37	61.6
Female	23	38.3
Total	60	100

In table 2, of the 60 babies, 37 were males and 23 females, which correspond to 61.6% of male and the rest female babies in table 2.

Table 3: Distribution of gestational age

Gestational age	No. of patients	Percentage
Preterm	21	35
Term	39	65
Total	60	100

In table 3, out of the 60 babies 39 were term babies, which corresponds to 65% and 35% of pre-terms.

Table 4: Clinical profile distribution among study population according to Apgar score

Apgar score	No. of patients	Percentage
Score > 7 Generally Normal	13	21.6
Score of 4-6; fairly low	31	51.6
Scores ≤3; critically low, needs intervention	16	26.6
Total	60	100

In our study, maximum patients, i.e., 51.6% (n = 31) were having Apgar score of 4-6 followed by ≤3 score were26.6% and least were > 7 score were 21.6% in table 4.

Table 5: Distribution of MRI changes in study population with stage2 HIE

Site of Lesion	Percentage
Corpus Callosam	31.6
BG/thalamus	21.6
No Change	13.3
PVL	23.3

In HIE 2 cases, 31.6% had involvement of corpus callosam. 23.3% had PVL, 21.6% had basal ganglia or thalamus lesion. There was no MRI evidence of HIE in 13.3%.

Table 6: Distribution of MRI changes in study population with stage 3 HIE

Site of Lesion	Percentage
Bilateral BG	55
Bilateral thalami	30
Subcortical white matter	15

Out of 6 babies with stage 3 HIE, 55% had involvement of bilateral basal ganglia.

30% had bilateral thalami lesion and the rest showed subcortical white matter lesion.

Discussion

Neonatal encephalopathy results from a variety of conditions; hypoxic-ischaemic brain injury is most important and is called hypoxic-ischemic encephalo-pathy (HIE). [8]

HIE is one of the most common causes of cerebral palsy and other severe neurologic deficits in children, occurring in two to nine of every 1000 live births. [9] Perinatal asphyxia is the most important cause of HIE, resulting in hypoxemia and hypercapnia. Hypotension and the resulting decreased cerebral blood flow lead to a cascade of deleterious events, including acidosis, release of inflammatory mediators and excitatory neurotransmitters, free radical formation, calcium accumulation, and lipid peroxidation.

These biochemical substances result in loss of vascular auto regulation in the setting of cerebral hypoperfusion. These "events" result in biphasic energy failure, in which initial impairment of cell metabolism is followed by reperfusion prior to eventual neuronal cell death. [10-15] Accurate identification and characterization of the severity, extent, and location of brain injury rely on the selection of appropriate neuroimaging modalities, including ultrasonography (US), computed tomography (CT), and magnetic resonance (MR) imaging. Newer diagnostic techniques such as diffusion-weighted MR imaging and MR spectroscopy provide further insight into HIE and the potential for possible therapeutic intervention.[16] Early diagnosis helps in management, prognosis and also in counseling the parents. MRI is the optimum modality of diagnosis in HIE. In our study, out of the 60 patients who were enrolled in the

study, our study shows male preponderance. According to a study by Flodmark O et al, there was no gender predilection. [17] Male gender being a risk factor for HIE has also been reported by other studies. [18] Our study shows, that term babies are more affected by MRI than preterms it may be because neonatal brain injury is difficult to diagnose in premature infants because either obvious signs are absent or if present, are attributed to developmental immaturity. [19] Preterm infants can also suffer from hypoxic ischemic encephalopathy, but, most often the change is not recognized early. For preterms findings will be obvious when MRI is done at corrected gestational age. Significantly higher numbers of primi gravida mothers in the affected babies are seen. It may be because the first delivery is more difficult than the subsequent ones. This points to the importance of intrapartum factors in the causation of HIE. In this study 70% of mothers belong to low socioeconomic group which has been found also by other authors. [20] In our study, 65% of term babies had changes in basal ganglia and/or thalamus. Other authors have also observed this finding. [21] This is because basal ganglia and thalami are metabolically very active in the immature brain. Occasionally severe basal ganglia lesions are seen with less obvious precipitating events. This may reflect failure to recognize the severity of asphyxia or due to individual susceptibility to damage because of previous hypoxic ischemic events or underlying metabolic or thrombotic disorders. Term infants who develop HIE following a well-defined acute hypoxic injury typically sustain bilateral lesions within the basal ganglia and thalami. In this study, out of the six babies with clinical stage 3 HIE 55% of them had bilateral basal ganglia involvement and 30% had bilateral thalami involvement. In stage 2 HIE no stage specific change in MRI could be found. Preterm brain is highly susceptible to injury including periventricular leucomalacia, intraventricular hemorrhage/ germinal layer hemorrhage and parenchymal hemorrhagic infarction. In this study 23.3% of preterm babies had periventricular leucomalacia. Also, MRI suggestive of hemorrhage was seen in preterm babies only which constitute 7.4% of all babies with positive MRI.

Limitation of the study

As mentioned previously there are limitations to our study as well first being the timing of the MR imaging examinations, taking place up to several months after birth. However, in most cases of perinatal asphyxia, the exact time of the inciting event is difficult to determine. Another limitation is that we did not perform initial imaging at birth around the time of insult normal. Finally, because of the heterogeneity of the group we studied, showing various injury patterns, the number of infants with specific injury patterns was limited. No predictive values of either ADC or DWI could be assessed.

Conclusion

MRI, as the most effective method for detection of hypoxic-ischemic lesions, is increasingly often used for the CNS diagnostics in preterm neonates, neonates with very low birth weight, and term neonates with significant perinatal history. Correct radiological diagnosis can truly contribute to the efficient implementation of care over the sick child. We can predict the infant development based on the MRI pattern of hypoxic-ischemic lesions, however, we cannot forget about the amazing malleability/flexibility of the child brain that can surprise both radiologists and clinicians.

References

1. Barkovich AJ, Hajnal BL, Vigneron D et al: Prediction of neuromotor outcome in perinatal asphyxia: evaluation of MR scoring systems. Am J Neuroradiol, 1998; 9: 143–49.
2. Rutherford M: The asphyxiated term infant. In: TMR of the neonatal brain. Rutherford M (ed.), W.B. Saunders, London-Toronto, 2002; 99–128.
3. Barkovich AJ, Westmark K, Partridge C et al: Perinatal asphyxia: MR findings in the first 10 days. Am J Neuroradiol, 1995; 16: 427–38.
4. Maller AI, Hankins LL, Yeakley JW et al: Rolandic type cerebral palsy in children as a pattern of hypoxic-ischemic injury in the fullterm neonate. J Child Neurol, 1998; 13: 313–21.
5. Okumura A, Kato T, Kuno K et al: MRI findings in patients with spastic cerebral palsy. II: Correlation with type of cerebral palsy. Dev Med Child Neurol, 1997; 39: 369–72.
6. Mutch L, Alberman E, Hagberg B et al: Cerebral palsy epidemiology: Where are we now and where are we going. Dev Med Child Neurol, 1992; 34: 547–51.
7. Bonifacio SL, Glass HC, Vanderpluym J et al: Perinatal events and early magnetic resonance imaging in therapeutic hypothermia. J Pediatr, 2011; 158: 360–65.
8. Zupan-Simunek V, Rutkowska M, Bekiesińska-Figatowska M: Wartość predykcyjna rezonansu magnetycznego (MR) w nabytych uszkodzeniach

mózgu u noworodków. Med Wieku Rozwo jowego, 2011; 15(3 Pt 2): 385–93
9. Norton L., Hutchison R.M., Young G.B., Lee D.H., Sharpe M.D., Mirsattari S.M. Disruptions of functional connectivity in the default mode network of comatose patients. Neurology. 2012; 78:175–181.
10. Els T., Kassubek J., Kubalek R., Klisch J. Diffusion-weighted MRI during early global cerebral hypoxia: a predictor for clinical outcome? Acta Neurol Scand. 2004;110:361–367.
11. Forbes K.P., Pipe J.G., Bird R. Neonatal hypoxic ischemic encephalopathy: detection with diffusion-weighted MR imaging. Am J Neuroradiol. 2000; 21:1490–1496.
12. Takahashi S., Higano S., Ishii K. Hypoxic brain damage: cortical laminar necrosis and delayed changes in white matter at sequential MR imaging. Radiology. 1993;189:449–456.
13. Siskas N., Lefkopoulos A., Ioannidis I., Charitandi A., Dimitriadis A.S. Cortical laminar necrosis in brain infarcts: serial MRI. Neuroradiology. 2003; 45:283–288.
14. Triulzi F, Baldoli C, Righhini A: Neonatal hypoxic-ischemic encephalopathy. In: Pediatric Neuroradiology. Brain. Tortori-Donati P, Rossi A, Biancheri R (eds.), Springer, Berlin-Heidelberg, 2005; 234–55.
15. Sie LTL, van der Knaap MS, Oosting J et al: MR patterns of hypoxicischemic brain damage after prenatal, perinatal or postnatal asphyxia. Neuropediatrics, 2000; 31: 128–36.
16. Valk J, Vermeulen RJ, van der Knaap MS: Post-hypoxic-ischemic encephalopathy of neonates. In: Magnetic resonance of myelination and myelin disorders. van der Knaap MS, Valk J. Springer-Verlag Berlin Heidelberg, 2005; 718–48.
17. Flodmark O, Barkovich AJ: Imaging of the infant brain. In: The newborn brain. Lagercranz H, Hanson M, Evrard P, Rodeck C (eds.), Cambridge University Press, 2002; 289–316.
18. Campistol J, Poo P, Fernandez Alvarez E et al: Parasagittal cerebral injury: magnetic resonance findings. J Child Neurol, 1999; 14: 683– 85.
19. Martin E, Barkovich AJ: Magnetic resonance imaging in perinatal asphyxia Archives of Disease in Childhood, 1995; 72: F62–70.
20. Pasternak JF, Gorey MT: The syndrome of acute near-total intrauterine asphyxia in the term infant. PediatrNeurol, 1998; 18: 391–98.
21. Tong KA, Ashwal S, Obenaus A et al: Susceptibility-weighted MR imaging: a review of clinical applications in children. Am J Neuroradiol, 2008; 29: 9–17 14.

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