AUDITORY BRAINSTEM RESPONSE IN NEONATES WITH HYPOXIC-ISCHEMIC-ENCEPHALOPATHY FOLLOWING PERINATAL ASPHYXIA

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ABSTRACT

The technique of auditory brainstem evoked responses testing (ABR) was applied to twenty four new born infants with asphyxia complicated by hypoxic-ischemic-encephalopathy (HIE) in an attempt to study potential influence of HIE on hearing impairment. Twenty normal term neonates with no apparent neurological disorder, were also examined for comparison.

Twenty two per cent (n=5) of the patients with HIE showed some abnormality in the ABR pattern, the major one being a transient elevation in threshold of wave V (n = 4; 16.6%). ABR abnormalities, however, were found with greater frequency in neonates with severe HIE (Stage III) than in those with Stage II HIE (75% vs 10%, p <0.001). Further ABR abnormalities were found in Stage II HIE only when duration of neurological abnormalities was >5 days. There was no difference, however, between the ABR latencies of the asphyxiated and non-asphyxiated newborn infants (p >0.05).

One neonate (4%) with severe HIE, however, had persistent ABR abnormality in the form of bilateral absence of all waves in the later part of the ABR with preservation of wave I. This implied only cochlear functions and absence of any brainstem conduction.

These results indicate that birth asphyxia complicated by HIE is a significant high risk factor for hearing impairment in the affected neonates. This justifies ABR testing of neonates with HIE (particularly Stage III), at the time of their discharge, as a screening procedure for early detection of permanent hearing loss.

Key words: *Perinatal asphyxia, Hypoxic-ischemic encephalopathy, Auditory brainstem responses.*

Birth asphyxia (low Apgar score) is one of the adverse perinatal clinical events that place the affected neonate at an increased risk of hearing impairment(1). Hypoxic-Ischemic-Encephalopathy (HIE), as demonstrated histopathologically in neonates dying of asphyxia, has damaging effects on various brainstem nuclei and inferior colliculi which participate in the formation of auditory brainstem response (ABR)(2,3). Some authors have demonstrated an elevated auditory threshold (*i.e.,* minimal intensity of click stimulus required to elicit a wave V of the ABR) as the predominant ABR abnormality in neonates with birth asphyxia(4-5) while others have found absence of all waves in the later part of the ABR with sparing of wave I(6-7). However, a few studies maintain that there is no permanent hearing loss in animals(8,9) or human neonates(10) subjected to prolonged hypoxia. The present study was designed to evaluate patterns of ABR abnormalities in neonates with HIE

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following birth asphyxia as compared with normal newborns.

Material and Methods

Twenty four term neonates with hypoxic ischemic encephalopathy (HIE) following birth asphyxia (Apgar <6 at 1 and 5 min)(11,12), who were admitted to the Neonatal ICU of Safdarjang Hospital during March 1989 to November, 1989, were examined by the ABR test (just after their general condition was stabilized) at the Electroneurodiagnostic Centre after an informed consent was obtained from the parents. Neonates with clinical factors such as low birth weight (<1500 g), hyperbilirubinemia requiring exchange transfusion, or phototherapy, intrauterine infections, sepsis, or meningitis, aminoglycoside administration, and craniofacial malformations were excluded from the study. Those having low Apgar scores without subsequent HIE were also not included. Sarnat and Sarnat(13) classification was used for grading of HIE and neonates were grouped into mild (Stage I), moderate (Stage II) and severe (Stage III) HIE. The mean age of asphyxiated (+HIE) infants studied was 8 ± 3.0 days.

Further, 20 normal term neonates, who had normal birth records and were apparently free from any neurological disorder, were also examined. The mean age of control infants studied was 9.0 ± 2.0 days.

The test was performed in a quiet room in the afternoon after they were fed and most of them were in natural sleep. Those awake were given 20 mg/kg of triclofos orally. Active electrodes were attached to the ipsilateral mastoid region and was referenced to a vertex electrode. Ground electrode was put on the forehead. The resistence was kept below 5000 ohms. Right and left ears were tested separately with rarefaction clicks of 0.1 msec duration administered at the rate of 50 per second, with masking noise on the other ear from the TDH-39P headphone, held lightly over the test ear. Four thousand responses were averaged with filter setting of 100-3000 Hz on the NDI equipment. Minimum of two tests were performed for reproducibility. Initially, the high intensity of 75 dB nHL was administered (nHL was determined on 20 normal individuals and was taken to be 30 dB for all infants) and the latencies, which were the intervals between the stimulation point and the peak of each wave were determined. Then, the intensity was decreased in steps of 15 dB nHL, till 30 dB nHL click, which was taken to be normal threshold of producing wave V. Wave V was identified by a peak after 6 msec followed by a deep terminal downstroke (slow negativity, *i.e.*, SN) carrying well below the baseline which is a useful mark of identification for wave V(14).

An infant was considered to have passed the test if wave V was present at 30 dB nHL in both ears or in one ear at 30 dB and the other ear at 45 dB nHL (3,6,15). The infants who passed the initial test were not asked to return for followup. The fail group was divided into "fail 30" and "fail 45" depending on absence of wave V in both ears to 30 dB and 45 dB nHL click respectively. The "fail 30" group had a clear wave V in at least one ear to 45 dB nHL. The fail groups were asked for repeat testing after a period of three months.

Gestational age was calculated in each child from the first day of last menstrual period and confirmed by physical and neurological criterion(16).

Statistical methods included calculation of 'p' value by Student 't' test and proportion testing.

Results

The auditory brainstem responses of 24 newborn infants with HIE were compared with the responses of 20 term healthy neonates, who had comparable birth weights and conceptional ages (gestational age + age after birth) (*Table I*). Further, as evident from *Table I*, there was no significant difference between the latencies of the ABR in normal and asphyxiated (+HIE) newborns ($p > 0.05$).

Wave V was consistently present at 30 dB nHL click stimulus in all the normal neonates ("pass-30"; normal threshold). *Fig. 1* shows a typical ABR record in a healthy term neonate. As evident, wave V is discernible down to 30 dB nHL click stimulus. Auditory threshold, however, was elevated in 4 (16.66%) of the neonates with HIE, two classified as "fail-30" and two "fail-45".

ABR abnormalities, however, were found with greater frequency in neonates with severe HIE (Stage III) than in those with Stage II HIE (75% vs 10%, $p < 0.001$) (*Table II*). Further, as evident from *Table II*, ABR abnormalities were found in Stage II HIE only when duration of neurological abnormalities was more than 5 days.

One neonate (4.1%) with severe HIE had bilateral absence of all waves in the later part of the ABR with preservation of wave I. This implied only cochlear functions and absence of any brainstem conduction. ABR abnormalities in this infant

TABLE I—*Latencies and S.D. of ABR in Asphyxiated (+HIE) and Normal Neonates*

Parameters		Neonates with HIE risk category	Normal neonates
No. of infants		24	20
Conceptional age (WK) (mean ± SD)		38-42 (40.6 ± 0.6)	38-42 (40.8 ± 0.8)
Birth weight (g) (mean ± SD)		2790 ± 250	2840 ± 280
Apgar score (Mean ± SD)	1 min	4.82 ± 0.34	8.47 ± 0.44
	5 min	5.14 ± 0.30	8.98 ± 0.50
ABR latencies (at 75 dB nHL click stimulus) (Mean ± SD) (ms)			
Wave I		1.94 ± 0.06	1.96 ± 0.05
Wave III		5.02 ± 0.16	5.10 ± 0.19
Wave V		6.98 ± 0.10	7.10 ± 0.08
I - V IPL		5.04 ± 0.08	5.14 ± 0.09

None of the differences for ABR latencies were significant ($p > 0.05$).

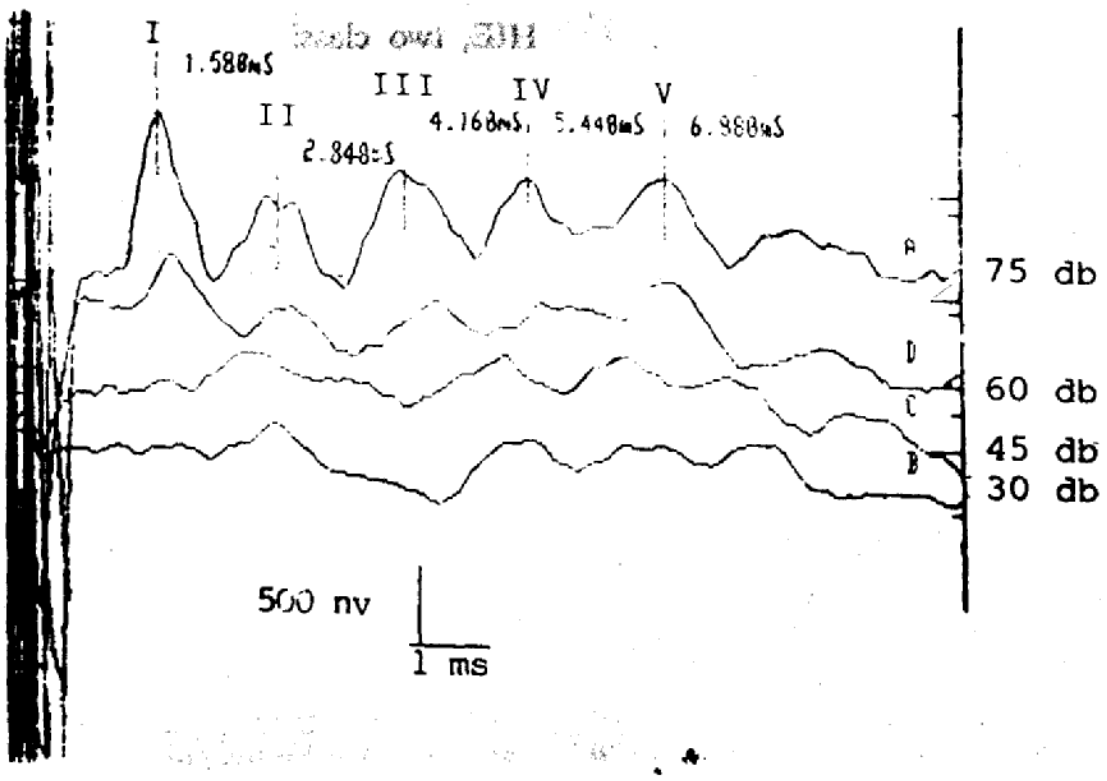

Fig. 1. Normal ABR record in a term, healthy neonate. Wave V is recordable down to 30 dB nHL click stimulus (normal threshold).

persisted on follow up for 6 months (*Fig. 2*). All the remaining infants, however, developed a normal hearing threshold on follow up pretesting at 3 months.

Discussion

The usefulness of ABR as a diagnostic tool in NICUs has only recently been recognized (3,5-6,15,17,18). Seven positive waves are observed in ABR and the origin of each wave is thought to be as follows: wave I is known to be the compound auditory nerve action potential and is similar to the action potential recorded in electrocochleography; wave II originates in the cochlear nucleus; wave III in the superior olive in the pons; wave IV in the lateral lemniscus; wave V in the inferior colliculi in the pons; while the origins of waves VI and VII are unknown(3).

The factors that place the affected neonates at an increased risk of hearing loss have been variously provided by Joint Committee on Infant Hearing, American Academy of Pediatrics(1). Despite their suggestion that severe birth asphyxia is a high risk factor for hearing impairment in neonates, there have been only limited information in humans on this aspect. This suggestion is supported by a number of experimental studies in animals(7) and histopathological evidence of anoxic-ischemic damage to inferior colliculi in monkeys(19) and human neonates(2). Further, some experimental studies have denied any role of hypoxia in producing permanent hearing impairment in animals(8,9). However, animal studies may not always be predictive of human response. This prompted us to

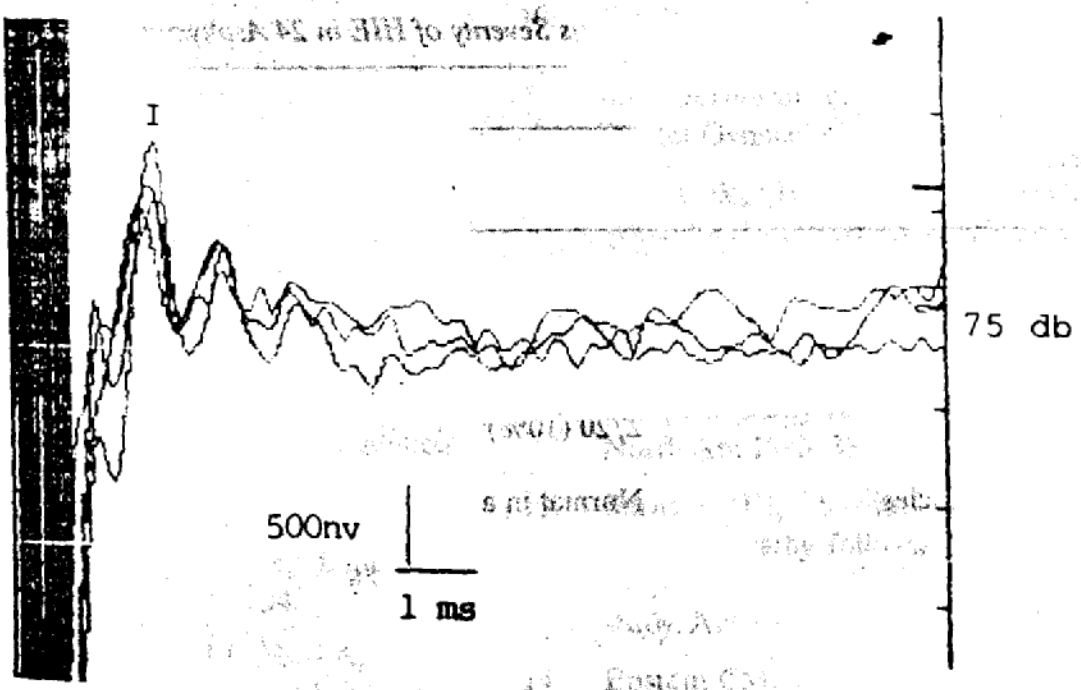

Fig. 2. ABR record (Rt ear) from a newborn with asphyxia and HIE: only wave I of the response is recordable (cochlear functions) but no brainstem conduction is present.

carry out ABR testing of asphyxiated neonates at the time of their discharge to detect the pattern of ABR abnormality in HIE.

In the present study on initial ABR testing abnormal results were detected in 5 (21.7%) of the asphyxiated newborns with the predominant abnormality being elevated auditory threshold (n=4, 16.6%). ABR abnormalities, however, were strongly correlated to severity (Stage III HIE) and duration (>5 days Stage II HIE) of neurological abnormalities in affected neonates ($p<0.001$). Yasuhara *et al.* in a similar study on asphyxiated neonates also found an increase in auditory threshold in 66.7% cases(4). However, on follow up retesting at 3 months, in the present series, all neonates developed a normal hearing threshold.

That hypoxia may produce only transient ABR abnormalities is also substantiated by the results of some experimental studies in animals(8). However, one neonate with Stage III HIE had persistent ABR abnormality in the form of absence of brainstem conduction with preservation of cochlear functions. The most likely mechanism for sparing of wave I while the brainstem components of the ABR are abolished in HIE is based on the hypoperfusion of blood flow to brainstem and preferential flow of blood through the internal auditory artery into the cochlea since the intra cochlear pressure (perilymphatic) is slightly lower than the intra cranial pressure, probably due to the presence of cochlear round and oval windows serve as pressure releasers. Thus, a significant blood flow to the cochlea is maintained even in severe hypoxemia with the resultant sparing of wave I(7).

However, as demonstrated by Barden and Pertzman(10), we too could not find any significant difference between the

TABLE II—*ABR Abnormalities Versus Severity of HIE in 24 Asphyxiated Neonates*

ABR parameter	Grading of HIE	
	Stage II (Moderate HIE) (n = 20)	Stage III (severe HIE) (n = 4)
(A) *Initial ABR testing*		
Normal ABR	18/20 (90%)	1/4 (25%)
Abnormal ABR	2/20 (10%)	3/4 (75%)
Wave I latencies	Normal in all subjects	Normal in all subjects
I - V IPL (BRAINSTEM Conduction Time at 75 dB nHL)	Normal in all subjects	Normal in 3 subjects. In one subject there was bilateral absence of all the waves in later part of the ABR with preservation of only wave I
Auditory threshold	Normal in 18 subjects (Stage II < 5 days) Elevated in 2 subjects (fail -30) Stage II ≥ 5 days)	Elevated in 2 subjects (both "fail = 45)"
(B) *Follow-up testing* at 3 month	All abnormalities reverted back to normal	Persistent absence of all waves in later part of the ABR (except wave I) in one subject. In remaining subjects ABR abnormalities reverted back to normal

Stage II HIE (Lethargic baby with mild hypotonia, sluggish NNR, focal or multifocal seizures, bradycardia, miosis).

Stage III HIE (Stuporous baby, with generalized flaccidity, absent NNR and decerebration).

mean latencies of the ABR in asphyxiated and nonasphyxiated infants. In conclusion, birth asphyxia complicated by HIE is a significant high risk factor for producing hearing impairment in the affected neonates. The incidence of permanent hearing loss of 4% as observed in the present study justifies BERA as a screening procedure for early detection of hearing impairment in the neonates surviving HIE (particularly prolonged stage II HIE, or stage III HIE) following an asphyxiating perinatal insult.

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