BRAINSTEM AUDITORY EVOKED RESPONSE IN NEONATES WITH BIRTH ASPHYXIA

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Manuscript received: May 21,1996; Initial review completed: June 24,1996; Revision accepted: October 7,1996

Objective: *To determine the brainstem auditory evoked response (BAER) abnormalities and their reversibility in neonates with birth asphyxia.* ***Design:*** *Prospective case control study.* ***Setting:*** *Tertiary care teaching hospital.* ***Methods:*** *30 term Neonates with 5-min Apgar < 6 and hypoxic ischemic encephalopathy (HIE) underwent BAER testing with follow up at 3 months. An equal number of normal term neonates served as controls. Results: 13 out of 30 (43.3%) neonates with birth asphyxia showed some abnormality in BAER wave form. The commonest type of BAER abnormalities seen were transient prolongation of latencies of various waves (69.2%) and prolonged interside latency difference (69.2%). Other abnormalities observed were prolonged interwave interval (23.1%) and prolonged interside interval difference (7.7%). Abnormalities in* BAER *were significantly associated with stages of HIE and duration of neurological abnormalities more than 5 days. On follow up of 16 cases at 3 months of age, BAER abnormalities reverted back to normal in all the neonates. The Denver Developmental Screening Test (DENVER II) was suspect in 4 cases but the BAER was normal.* ***Conclusion:*** *BAER abnormalities in asphyxic neonates are transient and revert back to normal at 3 months of age.* BAER *does not appear to be a useful tool for early detection of neurological handicaps.*

Key words: *Birth asphyxia, Brainstem auditory evoked response.*

THE consequences of perinatal asphyxia range from death to various degree of neuro-developmental sensory or motor deficits. One of its well known sequelae is sensorineural hearing impairment(l). Histopathological studies have provided evidence that brainstem of the human neonate is highly vulnerable to anoxia with a predominant damaging effect on various brainstem nuclei and inferior colliculi which participate in formation of auditory brainstem response(2). The brainstem auditory evoked response (BAER) has proved useful in determining the hearing threshold in even very young uncooperative patients(l,3,4). Further, BAER is not significantly altered by the state of consciousness, drugs and a variety of environmental factors including other sensory input to the cortex(5). Because of these properties, the BAER appears exceptionally well suited for **a** study of birth asphyxia. The present study was conducted to evaluate the pattern of BAER abnormalities and their reversibility in neonates with birth asphyxia.

Subjects and Methods

Term neonates with a 5 minute Apgar <6 and clinical signs of hypoxic ischemic encephalopathy (HIE) were enrolled for the study. There were 37 neonates who fulfilled the entry criteria, but in 7 BAER could not be performed because 4 died and 3 left the hospital before testing. The patients excluded were comparable to those included, in terms of birthweight, gestation and severity of HIE. Thirty normal term neonates with uneventful prenatal, natal and postnatal period, were evaluated as controls. Preterms, neonates with low birth weight (<2500 g), hyperbilirubinemia requiring exchange transfusion or phototherapy, intrauterine infections, sepsis or meningitis, aminoglycoside administration and craniofacial malformations were excluded from the study.

Gastational age was calculated from the first day of last menstrual period and confirmed by physical and neurological criteria (6). The gestational age ranged from 38.0-41.6 week with a mean of 39.2 weeks and the mean post natal age was 8 ± 3 days in the study group. For controls, gestational age ranged from 37.4 - 41.2 weeks with a mean of 39.5 weeks and the post natal age was 7 ± 2 days. Sarnat and Sarnat classification was used for grading the severity of HIE(7). Out of 30 neonates, maximum (n-20) were in Stage II, six in Stage III and 4 in Stage I. The duration of symptoms was less than or equal to 5 days in 18 patients, and more than 5 days in 12 cases.

BAER was done as soon as possible after their general condition stabilized. BAER test was performed by using the technique described by Taylor *et al.(8).* Before performing the BAER test, all babies were examined for local ear abnormalities. The test was performed in a quiet room after they were fed and were in natural sleep. Those awake were given 20 mg/kg of triclofos orally. Silver-silver chloride electrodes were used. The electrodes were applied according to International 10-20 system of electrode placement(8). Active electrode was applied over the vertex, with reference electrodes at the mastoid and ground electrode on the forehead. The resistance was kept below 5000 ohms. Recordings were obtained by computerized electric response audiometer, Neuropack Four Machine (Nihon Kohden, Japan). The sweep velocity was 10 ms, click acoustic stimuli with a click rate of 10/second alternating in polarity were presented by an earphone to each ear alternately at an intensity of 90 dB hearing level. A masking sound of 40 dB was given to the nonstimualted ear, a two channel recording was done after stimulation of each ear. The electrical activity was filtered and averaged to 4000 responses.

Auditory threshold was recorded for right and left ears separately with rarefaction clicks of 0.1 msec duration administered at the rate of 50 per second with a sweep velocity of 20 msec. Four thousand responses were averaged and a minimum of two tests were performed for reproducibility. Initially 74 dB nHL was administered, then intensity was decreased and recordings were made on 60 dB, 44 dB and 30 dB. Intensity of 30 dB was taken as the normal threshold for wave V.

The records were analyzed in terms of auditory threshold, latency, interside latency difference (difference between latencies of either waves obtained from stimulation of right and left ear) and interwave interval and interside interval difference (difference in interpeak intervals obtained from stimulation of right and left ear). The values of the parameters under study were said to be abnormal when they exceeded 3SD above mean value in the control group.

Follow up was done at the age of 3 months, only in the study group. No selection criteria was used. Only 16 out of 30 patients turned up for follow up during the specified period despite postal reminders and home visits; wherever possible. Denver developmental screening test (DENVER-II)(9) was used to assess the gross motor, language, fine motor-adaptive and personal-social development of the child and BAER was performed in all.

Statistical analysis was done using Student's 't' test. Univariate analyses (Chi square test for association and trend and Fischer's exact test) were also done to evaluate the significance of association between evoked response abnormalities and various neonatal factors.

Results

The latencies and interwave intervals of different waves in both cases and controls are shown in *Table I.* The mean latencies of various waves in BAER was significantly higher in cases as compared to controls. However, the difference in mean interwave intervals in cases and controls was not significant statistically. On considering a value 3SD above the mean value in the control group as the criteria for a parameter under study to be positive, 13 out of 30 (43.3%) neonates with birth asphyxia showed some abnormalities in one or the other wave forms. Of various types of abnormalities, prolonged latency and prolonged interside latency difference were commonest and were present in 9 cases out of 13 (69.3%) each. Other abnormalities observed were prolonged interwave interval in 23.1% and prolonged interside interval difference in *7.7%* of neonates with HIE.

Univariate analysis showed that among various neonatal factors, only stages of HIE and duration of neurological symptoms more than 5 days were significantly associated with auditory evoked response abnormalities *(Table II).*

TABLE I–*Latencies of Various Waves and Interwave Intervals on BAER at 90 dB nHL (in msec)*

Parameter	Controls (n = 30)		Cases (n = 30)	
	Mean	SD	Mean	SD
Latency				
I	1.69	0.17	1.83	0.34*
II	2.83	0.25	3.09	0.42**
III	4.50	0.26	4.75	0.45**
IV	5.63	0.38	5.88	0.47**
V	6.77	0.39	7.10	0.60**
Interwave interval				
I-III	2.81	0.28	2.92	0.35
III-V	2.28	0.26	2.34	0.35
I-V	5.08	0.39	5.26	0.55

* and ** represent significant differences between cases and controls (* $p < 0.01$; ** $p < 0.001$).

TABLE II–*Univariate Analysis of Various Neonatal Factors and BAER Abnormalities*

Neonatal factors		BAER		
	(n=30)	Normal	Abnormal	p Value
1. *Sex*				
Male	22	13	9	
Female	8	4	4	>0.05
2. *Birth weight* (kg)				
≥ 2.5 kg	16	11	5	
< 2.5 kg	14	6	8	>0.05
3. *Stage of HIE*				
I	4	4	0	
II	20	12	8	
III	6	1	5	0.06*
4. *Duration of neurological symptoms (days)*				
≤ 5	18	13	5	
> 5	12	4	8	<0.05

* Borderline significant (p=0.06) for a comparison of stage III with a combination of Stages I and II by Fischer's exact test.

Out of 30 cases, only 16 (53.3%) returned for follow up at the mean age of 12.3 ±2.1 weeks. Out of these, 7 patients had an abnormal BAER at initial testing. Follow up BAER revealed that all the abnormalities on initial testing had become normal in all the subjects *(Fig. 1)*.

Evaluation of developmental status (Denver II) at the end of follow up (3 months age) revealed that neurological development was abnormal in 4 out of 16 neonates. Out of these 4 suspects, 3 had HIE Stage III and one had prolonged HIE Stage II (8 days). All these 4 suspects had initial BAER abnormalities but on follow up none of these had abnormal BAER recording despite clinical evidence of a neuro-developmental abnormality.

Discussion

Early detection of hearing loss by conventional audiologic testing is difficult and usually can not be done until the child is 2 to 3 years old. The utilitiy of brainstem evoked responses as a diagnostic tool in neonates has been recognized only recently(10-13).

The prevalence of BAER abnormalities on initial testing in the present study was 43.3%. This is comparable to an earlier report(14) but lower than that reported (89%) from another study(15). The reason for this discrepancy may be explained by the fact that the latter study(15) had also included patients with intracranial hemorrhage. Another report from Delhi observed some

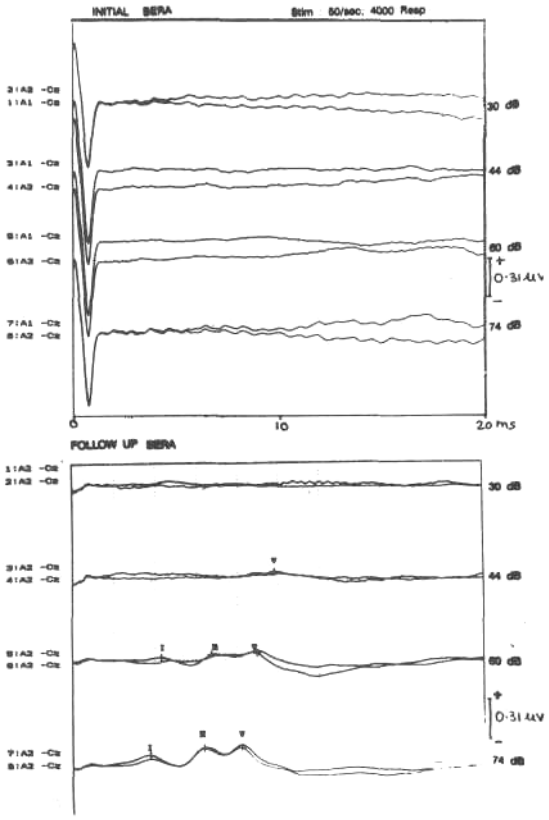

Fig. 1. Absent response on initial BAER becoming normal on follow up.

degree of BAER abnormalities in 22.0% of patients with HIE(3).

In the present study, the latencies of all the waves in neonates with birth asphyxia were significantly prolonged whereas interwave intervals did not show a significant change when compared with the neonates in control group. Earlier workers(l) have also observed that the latencies of various waves as well as the interpeak intervals were significantly prolonged in asphyxia. However, our findings are in contrast to reports(3,16) which did not find any significant alteration in the latency as well as interwave intervals in neonates with birth asphyxia.

In our study, elevated auditory threshold was present in 16.66% neonates, which is comparable to that reported earlier(3). However, another study(15) documented a higher prevalence of increased auditory threshold (66.7%) but their study group included premature babies also.

In majority of patients (66.7%) in the present study, the BAER abnormalities were suggestive of peripheral involvement rather than brainstem abnormality (prolonged latencies of various waves with normal interwave intervals). This observation is in contrast to experimental as well as clinical data, which suggest that various brainstem nuclei and inferior colliculi are most susceptible to asphyxia. However, BAER abnormalities similar to those reported in the present study have been documented earlier(17). Prolonged latencies with normal interwave intervals would suggest involvement of the cochlear nerve or the cochlea. However, it is difficult to differentiate by BAER alone between the two. Cochlear involvement in asphyxia has been observed clinically in asphyxiated infants(17) as well as in necropsy series(18). The reason for findings suggestive of cochlear involvement may be depression of endocochlear potential as a result of hypoxia and acidosis(19).

On follow up retesting at 3 months of age in 16 cases, all the BAER abnormalities became normal. The fact that hypoxia may produce only transient BAER abnormalities is substantiated by results of other studies done on human neonates(16) and some experimental studies in animals(20). These transient abnormalities have been attributed to middle ear effusion, collapse of ear canal, immaturity of peripheral neural structure or temporary insult like asphyxia. However, it is difficult to determine the exact cause of transient abnormalities of BAER.

It is concluded that BAER abnormalities in asphyxiated neonates are transient and revert back to normal at 3 months age. BAER does not appear to be a useful (sensitive and cost effective) tool for early detection of neurological handicaps in asphyxiated neonates.

REFERENCES

1. Kileny P, Connelly C, Robertson C. Auditory brainstem responses in perinatal asphyxia. Int J Pediatr Otorhinolaryngol 1980, 2:147-159.
2. Leech RW, Alvord EC. Anoxic-ischemic encephalopathy in human neonatal period: The significance of brainstem involvement. Arch Neurol 1977, 34: 109-113.
3. Anand NK, Gupta AK, Raj H. Auditory brainstem response in neonates with hypoxic ischemic encephalopathy following perinatal asphyxia. Indian Pediatr 1991, 28: 901-907.
4. Deorari AK, Garg R, Bisht MS, Ahuja GK, Paul VK, Singh M. Auditory brainstem evoked response in normal neonates and infants. Indian Pediatr 1989, 26: 981-986.
5. Mason S, McCormick B, Wood S. Auditory brainstem response in pediatrics audiology. Arch Dis Child 1988, 63: 465-467.
6. Dubowitz LMS. Dubowitz V, Goldberg C. Clinical assessment of gestation in newborn infant. J Pediatr 1970, *77:*1-10.
7. Sarnat HB, Sarnat MS. Neonatal encephalopathy following fetal distress: A clinical and electroencephalographic study. Arch Neurol 1976, 33: 696-705.
8. Taylor MJ. Evoked potentials in pediatrics. *In:* Evoked Potentials in Clinical Testing, 2nd edn. Ed. Halliday AM., London, Churchill-Livingstone, 1993, pp 489-521.
9. Frankenburg WK, Bodds J, Archer P, Shapiro H, Bresnick B. The Denver II: A major revision and restandardization of the Denver developmental screening test. Pediatrics 1992, 89: 91-97.
10. Deorari AK, Paul VK, Singh M. Birth asphyxia and neurodevelopmental outcome. Indian Pediatr 1989, 26: 793-799.
11. Despland PA, Galambos R. The auditory brainstem response (ABR) is a useful diagnostic tool in the intensive care nursery. Pediatr Res 1980,14:154-158.
12. Anand NK, Gupta AK, Raj H. BERA a diagnostic tool in neonatology. Indian Pediatr 1990, 27:1039-1044.
13. Galambos CS. Introduction: Brainstem evoked response audiometry in neonates. J Otolaryngol 1985, 4 (Suppl 14): 5-6.
14. Hecox KE, Cone B. Prognostic importance of brainstem auditory evoked response after asphyxia. Neurology 1981, 31: 1429-1433.
15. Yasuhara A, Kinoshita Y, Hori A, Iwase S, Kobayashi Y. Auditory brainstem response in asphyxiated neonates. Pediatr Neurol 1986, 2: 220-223.
16. Barden TR, Pertzman P. Newborn brainstem auditory evoked responses and perinatal clinical event. Am J Obstet Gynecol 1980,136: 912-919.
17. Galambos R, Despland PA. The auditory brainstem response (ABR) evaluates risk factors for hearing loss in the newborn. Pediatr Res 1980,14:1 59 -163.
18. Hall JG. The cochlea and the cochlear nuclei in neonatal asphyxia. Acta Oto-laryng 1964,194 (Suppl): 1-93.
19. Sohmer H, Freeman S, Gafni M, Goitein K. The depression of auditory nerve-brainstem evoked response in hypoxemia: Mechanism and site of effect. Electroenceph Clin Neurophysiol 1986, 64: 334-338.

20. Cycowixz Y, Schmuel M, Freeman's Wanszelbaum A, Sohmer H. Perinatal hypoxia and auditory brainstem response threshold: No evidence of permanent hearing loss. Hearing Research 1988, 33: 239-294.