BRAINSTEM AUDITORY EVOKED RESPONSE IN NEWBORNS WITH HYPERBILIRUBINEMIA

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Objective: *To determine the initial Brainstem Auditory Evoked Response (BAER) abnormalities in neonates with hyperbilirubinemia and the possible reversibility of abnormal BAER after therapy. Design: Prospective cohort study. Setting: Tertiary care hospital. Subjects:* 30 *term neonates with hyperbilirubinemia (S. bilirubin > 15 mg/dl) as cases and 25 normal term neonates as controls. Methods: Duration of study was from August 1995 to August 1996. BAER were recorded before therapy at peak hyperbilirubinemia, after therapy, and the age of 2-4 months using electric response audiometer (Nihon Neuropack Four Machine). Denver Development Screening Test (Denver 11) was performed at 1 year of age. Results: Seventeen out of thirty (56.7%) neonates with hyperbilirubinemia showed abnormalities on initial BAER. Commonest abnormality seen was raised threshold of wave V in* 22 *neonates (40%). Other abnormalities observed were absence of all waves at 90 dB (23.3%), prolongation of latencies of various waves* (26.7%) *and prolongation of various intervals* (26.7%). *Abnormalities in BAER correlated significantly with bilirubin level. After therapy abnormalities reverted back to normal in 10 cases but persisted in 7 out of 17 (41.17%) cases with initial abnormal BAER. Development screening at 1 yr was abnormal in 3 infants all of whom had persistent abnormalities in BAER. Conclusion: Serial BAER is a useful, non invasive tool to detect neurodevelopment delay secondary to neonatal hyperbilirubinemia.*

Key words: *Bilirubin encephalopathy, Brainstem auditory evoked response (BAER), Neonatal hyperbilirubinemia.*

BESIDES other sequelae, severe hyperbilirubinemia is particularly toxic for the auditory pathway and may result in sensorineural hearing loss(1-7). Clinicopathological studies have suggested that bilirubin encephalopathy affects superior olive, lateral leminiscus and inferior colliculus(8). However, objective methods to predict early CNS affection of bilirubin toxicity are not easily available.

The brainstem auditory evoked response (BEAR) is an effective and noninvasive means of assessing the functional status of the auditory nerve and the brain stem auditory sensory pathway(9). It is not significantly altered by state of consciousness, drugs and variety of environmental factors including other sensory input to the cortex(10). The BAER changes in response to hyperbilirubinemia include a loss of one or more peaks of waves I to V or an increase in latency of wave III or V or raised threshold(7,11-20).

The present study was undertaken to evaluate the effect of hyperbilirubinemia in term newborns on Brainstem auditory evoked response (BAER) and change if any in BAER after therapy.

Subject and Methods

Thirty consecutive term neonates (16 male, 14 female) who presented to the Neonatal Special Care Unit (NSCU) of Gandhi Memorial and Associated Hospitals, King George's Medical College, Lucknow from August 1995 to April 1996 with hyperbilirubinemia (total S. bilirubin level > 15 mg/dl) were included in study as cases. Twenty five normal term neonates with uneventful perinatal period and a peak serum bilirubin < 12 mg/dl were included as controls. Neonates born with birth asphyxia (Apgar < 7 at 5 minutes), intrauterine infections, sepsis or meningitis, aminoglycoside administration and craniofacial malformations were excluded from the study.

The mean birth weight of cases was 2.63 (± 0.16) kg and that of controls was 2.65 (± 9.21) kg. The mean age at entry into study was 4.2 (± 1.2) days in the cases and 3.9 (± 1.3) days in controls. Mean bilirubin level in cases was 22.4 (± 2.7) mg/dl and in controls was 7.7 (± 1.9) mg/dl. The cause of hyperbilirubinemia was idiopathic in 63.3%, Rh incompatibility in 10.0% and ABO incompatibility in 26.7% cases. Exchange transfusion was performed in 14, the rest needing only phototherapy. Two neonates were kernicteric at study time.

BAER Studies

Initial BAER was done within 3 hours of hospitalization after obtaining informed consent from the parents. In 6 patients it was done within 3-12h of initiation of therapy. BAER test was performed by using the technique described by Taylor *et al.(21).* Those neonates who were 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 electrodes placement(21). Recordings were obtained by computerized electric response audiometer, Neuropack Four Machine (Nihon Kohden, Japan). The sweep velocity was 10 m/sec. 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 were given to the 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 m sec duration administered at the rate of 50 per second with a sweep velocity of 20 m/sec. A total of 4000 responses were averaged and a minimum of two tests were performed for reproducibility. Intensity of 30 dB was taken as normal threshold for wave V.

Repeat BAER was done in all cases when serum bilirubin levels fell below 12 mg/dl. Mean interval between initial and repeat BAER was 4.2 ± 1.1 days. BAER was also done in controls at the mean post natal age of 3.9 ±1.9 days.

Follow up

All cases with hyperbilirubinemia were followed till the age of one year. Denver Developmental Screening Test (DENVER-II)(22) was used to assess gross motor, language, fine motor adaptive and personal social development of the child and BAER was performed in all.

The records were analyzed in terms of auditory threshold, latency and interwave intervals. The values of the parameters under study were said to be abnormal when they exceeded 2 SD above mean value in the control group. The hyperbilirubinemia

cases were stratified into three groups: (i) Group A - Serum bilirubin 15-20 mg/dl; (n) Group B - Serum bilirubin 21-25 mg/dl; and *(Hi)* Group C - Serum bilirubin >25 mg/dl.

Statistical analysis was done by Student's 't' test, paired Fisher's exact test and Chi square test for association and trend.

Results

The latencies and interwave intervals of different waves in controls and cases (both before and after therapy, namely, phototherapy or exchange transfusion) are shown in *Table I.* The mean latencies of various waves and mean interwave intervals in BAER were significantly higher in hyperbilirubinemia as compared to controls. Neonates with hyperbilirubinemia showed some abnormalities in one or other wave forms. In all the patients who had either absent response or raised threshold, the abnormalities were bilateral. One out of 9 (11.1%) neonates in Group A, 10 out of 15 (66.6%) neonates in Group B and all the 6

TABLE I— *Latencies of Various Waves and Interwave Intervals Before and After Therapy at 90 dB nHL (in m. sec.) (mean ± SD)*

	Controls	Hyperbilirubinemia		'P' value	
		Before therapy	After therapy		
	(a) (n = 25)	(b) (n = 30)	(c) (n = 30)	a *vs b**	b vs c**
Latency					
I	1.69 ±0.15	1.83 ±0.16	1.78 ±0.13	< 0.001	<0.05
II	2.86 ±0.20	3.03 ±0.20	2.91 ±0.25	< 0.001	< 0.001
III	4.50 ±0.25	4.83 ±0.26	4.62 ±0.26	< 0.00001	< 0.001
IV	5.66 ±0.42	5.95 ±0.30	5.70 ±0.24	< 0.001	<0.01
V	6.74 ±0.35	7.25 ±0.45	6.94 ±0.31	< 0.00001	< 0.0001
Inervals					
I-III	2.81 ±0.26	3.00 ±0.21	2.80 ±0.16	< 0.001	< 0.001
III-V	2.24 ±0.21	2.42 ±0.30	2.31 ±0.21	<0.01	<0.02
I-V	5.05 ±0.36	5.42 ±0.40	5.14 ±0.25	< 0.0001	< 0.001

*p value has been derived by Student 't' test.

**p value has been derived by paired T test.

Cutoff point taken for abnormal BAER is > 2 SD above mean for that variable in control group.

neonates in Group-C had bilateral abnormal responses on initial BAER denoting brainstem dysfunction.

There was no response in 23.3% cases. Commonest abnormalities were prolonged latency of wave V (26.7%), followed by prolonged wave III (23.3%), prolonged wave I (10%), prolonged interwave interval I-II (6.7%) and I-V (20%). Threshold was raised in 12 (40) cases, *i.e.,* responses were absent bilaterally at 30 dB.

Latency of different waves and intervals significantly decreased (returned towards normal) after therapy. When serum bilirubin levels came down *(Table I),* the abnormalities on initial BAER reverted back to normal in most cases (response remained absent in 2/7 cases, raised threshold persisted in 5/12 cases, latency remained prolonged in 1/8 cases and interval became normal in all cases).

Follow up BAER was done in 21 (70.0%) out of 30 cases (Group A-9, Group B-6, Group C-6) who returned for follow up at the mean age of 14.4 ± 2.2 weeks. Of the 15 patients who had an abnormal BAER on initial testing, in only 3 (14.3%) were there persistent abnormalities on BAER. All three had initial serum bilirubin levels > 24 mg/dl and two also had kernicterus.

Screening by Denver Development Screening Test (Denver II) at 1 year of age revealed that neurological development was normal in all the neonates of Group A, 88.9% of Group B, and 66.7% of Group C. All the 3 infants who showed abnormal development on Denver II also had abnormal BAER.

Discussion

BAER has been show to be an effective, objective method of assessing auditory pathway function (hearing as well as brainstem function) in neonates and infants and recently has been recognized as a useful diagnostic tool in neonates(23-25). Abnormalities of BAER following neonatal hyperbilirubinemia have been described earlier(7,11-20).

The frequency (56.7%) of BAER abnormalities in hyperbilirubinemia on initial testing in present study was comparable to some earlier reports(12,18) but higher than others (16%-33%)(13,17). Latencies of all the waves and intervals were significantly prolonged in hyperbilirubinemia as compared to controls showing affection of VIII nerve as well brainstem.

Most of the previous workers have shown the transient nature of the bilirubin encephalopathy in almost all patients after therapy but we observed reversal of abnormalities in most but not all after phototherapy and/or exchange transfusion. However persistent abnormality in a few patients was also documented by others(14).

To conclude, BAER detects subclinical bilirubin encephalopathy even before appearance of any sign or symptoms of kernicterus as observed in the present study. BAER abnormalities were transient in majority of patients and were significantly correlated with level of serum bilirubin and duration of jaundice. Thus serial BAER may be a useful, non invasive, cost effective and radiation free tool to detect neurodevelopment delay secondary to hyperbilirubinemia.

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