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A COMPARATIVE STUDY OF BRAINSTEM AUDITORY EVOKED POTENTIALS IN PRETERM AND FULL-TERM INFANTS

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Abstract : Background : Preterm infants can have many neurological problems. An enormous amount of fetal brain development occurs during the last trimester of pregnancy. They include myelination, glial cell migration and the development of a complex gyral pattern. The brain doesn't show the normal growth after birth in preterm infants. Brainstem auditory evoked potentials (BAEPs) are a noninvasive neurophysiologic assessment of brainstem maturation in babies.

Methods : BAEPs in 25 preterm and 25 full-term infants were considered for the study. Infants having history of birth trauma, metabolic disorders or intracranial infection were excluded. BAEP waveforms (absolute and interpeak latencies) were recorded and analyzed. Student t test was used to analyze the data thus acquired.

Results : Analysis of data revealed a significant increase in latency of BAEP waveform V ($P<0.05$). Other latencies and interpeak latencies of BAEP waveforms were comparable.

Conclusion : The preterm infants have a prolonged latency of BAEP waveform V suggestive of a retarded myelination of the central auditory pathway. Thus BAEP could be a useful electrophysiological test to assess neuronal myelination and maturation in preterm infants.

Key words : BAEPs central nervous system full-term maturation preterm

INTRODUCTION

Preterm births are on the rise in today's stress filled world and are one of the major causes of neonatal mortality and morbidity. Preterm infants are at an increased risk of complications, including disabilities and impediments in physical growth and mental development. A mild hearing impairment early in life can significantly affect the

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normal development of speech and language, if undetected for more than six months (1). It is therefore very important that premature neonates, who are at risk of hearing impairment, be evaluated during the neonatal period (2, 3). The BAEP is the most widely used and accurate technique for assessing hearing in neonates, but the BAEPs need to be recorded after the infants have reached term and before 3 months corrected age which is approximately 1 year after birth. During the preterm period, the BAEPs are not reliable predictors of audiological or neurological sequelae (2, 4).

Although the neuronal migration is complete by 20 weeks of gestational age, an enormous amount of the fetal brain development occurs during the last trimester of gestation, including myelination, glial cell migration and the development of a complex gyral pattern (5). In extremely preterm infants, neonatal brain injury and interruption of the normal maturation of the brain result in functional impairments that appear to manifest in the later life (6). The brains of preterm babies do not develop as well as those who are carried to full-term. In preterm babies, a part of the brain doesn't show normal growth after birth. In fact some parts of the preterm babies' fetal brain do not change from date of birth and even when they reach what would have been a full-term birth date (7). About 25 percent of extremely preterm babies present with neurological problems at 18 to 22 months, and 17 percent will develop cerebral palsy. As a result, preterm babies often die or suffer lifelong consequences including cerebral palsy, chronic lung disease and hearing loss. These neurological impairments posing lifelong threats can be evaluated in these preterm infants using neurophysiologic techniques, such as evoked potentials and event related potentials.

The clinical neurological evaluation is difficult in preterm infants. Evoked potentials provide an objective measure of the CNS function and thus can be an important adjunct to the clinical examination and a means to follow up brain growth and maturation in preterm infants. Brainstem auditory evoked potential (BAEPs) are noninvasive electrophysiological recordings and form an objective neurophysiologic assessment of auditory pathway and brainstem maturation in babies. BAEPs are obtained in response to repetitive auditory stimuli and can be recorded from the peripheral and central parts of the nervous system. BAEP recording is done to evaluate hearing in preterm infants and to study the neurologic maturation and integrity of the auditory pathway by comparing the latencies of the waveforms with that of the full-term babies.

BAEPs reflect the conduction along the auditory brainstem pathway. A recognisable BAEP can be recorded in preterm infants of 28-32 weeks of gestational age (8). The BAEP waveform in neonates is comprised of 3 identifiable waves (I, III, and V). Electrophysiological data in preterm infants have shown that wave I is generated peripherally in the auditory nerve. Wave III reflects the firing of axons exiting the cochlear nuclear complex in the brainstem. Wave V primarily reflects an action potential generated by axons from the lateral lemniscus at a more rostral brainstem location (9).

Studies on the brain maturation using BAEPs in preterm and full-term infants have shown conflicting evidences regarding the delayed neurologic maturation and its predictability in the preterm babies (2, 10, 11). As observed in these studies, the latencies of BAEP waveforms were delayed in preterm infants and that prematurity itself could affect these latencies (2, 10). Preterm birth also has a significant effect on the neurologic maturation and experience plays a crucial role in the developmental process. This conceives the probability that extra-uterine exposure to the environmental stimuli in the preterm could exert some effects on the maturation of the developing human brain (11). This implicates that BAEPs recorded in the premature period (at birth in a preterm infant) are not reliable predictors of audiological/neuronal maturation. Hence, the present study compares the neurologic maturation in preterm and full-term infants at one year of extra uterine age by recording BAEPs.

METHODS

BAEP data of 25 preterm and 25 full-term infants (50 subjects) of one year age were compared. The preterm infants were those born before 37 weeks of gestation and were referred from the Paediatric department for assessment of auditory functioning. The full-term infants were recruited from among those attending the Paediatric department for routine immunization and from the general population. The infants were studied at one year of their extra uterine age to compare the neurologic maturation in the preterm and full-term infants and also to assess any impairment. The data was acquired in the Department of Neurosciences, M. S. Ramaiah Medical College and Hospital from January 2006 to June 2008. Infants with a history of craniofacial anomalies, chromosomal disorders, TORCH (toxoplasmosis, other infections, rubella, cytomegalovirus infection, and herpes simplex) infection at birth, birth trauma, metabolic disorders or intracranial infections were excluded from the study. All the infants underwent audiologist evaluations to exclude those with altered hearing. Informed written consent was obtained from the parents/guardians of all infants. The study was approved by the institute's ethics committee.

Procedures:

BAEPs were recorded using Nihon Kohden Neuropack (MEB 2200 Version 03.02). The procedure was done in supine posture on the bed in a semi-darkened room, after a feeding and majority of the infants received sedation with promethazine orally of dose 0.5 mg/kg bodyweight. Electrode placing, nomenclature and methodology of BAEP recordings were according to Chiappa (1990) (12). The electrodes were arranged on the mastoid (reference), midline on high forehead or crown of the head (active), and shoulder (ground).

Recordings were obtained using silver cup electrodes filled with contact gel. The skin surface was prepared with abrasive gel, electrodes fixed and secured with adhesive plasters. At all recording sites, electrode impedance was kept below 5W. BAEP recording was performed on each ear using 80 dBHL clicks of alternating polarity presented monaurally. Broad band clicks are the only stimuli for infants and the click

intensity should be calibrated relative to normal hearing thresholds in the laboratories. The repetition rate of the stimulus was at a rate of 10/sec. A total of 2000 evoked responses were recorded and averaged for two trials each (to assess reproducibility) from the right and left ear. The earphone is to be held above the ear, because the weight of the earphone can collapse the ear canal in preterm infants. Broadband pass filters at 10 to 2500 Hz, restrictive filtering of 100-3000 Hz. The analysis time was 10 msec. Samples contaminated with artifacts were auto discarded.

The absolute mean latencies of BAEP waveforms I, III, V and interpeak latencies I-III, III-V, I-V were measured.

Statistical analysis (13, 14):

Two tailed independent student t test has been used to find the significance in latencies of BAEP waveforms and the interpeak latencies between the 2 groups. Paired Student t test has been used to find the significance of latencies of BAEP waveforms within each group and between right and left ear.

Statistical software: The statistical software namely SPSS 11.0 and Systat 8.0 were used for the analysis of the data and Microsoft word and Excel have been used to generate tables.

RESULTS

This comparative study consisted of 25 preterm and 25 full-term infants. The mean gestational age of preterm infants at birth were 35±2 weeks. BAEP parameters – Waveform I, III, V latencies, I-III, III-V, I-V inter-peak latencies recorded and averaged from the two groups were compared.

Figs. 1 and 2 show BAEP waveforms in the full term and preterm infants respectively after right and left ear stimulation with the marking of the prominent waves I, III, V marked.

The mean latency of BAEP waveform I in the preterm infants was 1.45±0.23 ms, 1.40±0.37 ms and in the term infants was 1.36±0.34 ms, 1.45±0.20 ms for the right and left ears respectively. (Table-I). The mean latency of BAEP waveform III in the preterm infants was 3.82±0.83 ms, 3.74±0.90 ms and in the term infants was 3.83±0.85 ms, 3.82±0.84 ms for the right and left ears respectively (Table-I).

Thus the mean pattern of absolute latencies of BAEP waveforms - I and III from right and left ears did not show significant difference between the two groups - preterm

TABLE II: Comparison of Mean Pattern of Inter-peak Latency of BAEP waveforms between the Preterm and Full-Term groups.

Inter-peak Latency (ms) (Mean±SD)	*Ear*	*Preterm*	*Full-Term*	*P value*
I–III	Right	2.47±0.31[a]	2.57±0.43[a]	0.367
	Left	2.35±0.55[a]	2.50±0.30[a]	0.427
III–V	Right	2.22±0.93[a]	2.13±0.92[a]	0.742
	Left	2.27±0.95[a]	2.09±0.96[a]	0.541
I–V	Right	4.60±0.36[a]	4.53±0.48[a]	0.613
	Left	4.45±0.98[a]	4.44±0.32[a]	0.957

Superscripts

1. Comparison with in each group – Right vs Left

i. Identical Superscripts (a vs a) are non-significant (P>0.05)

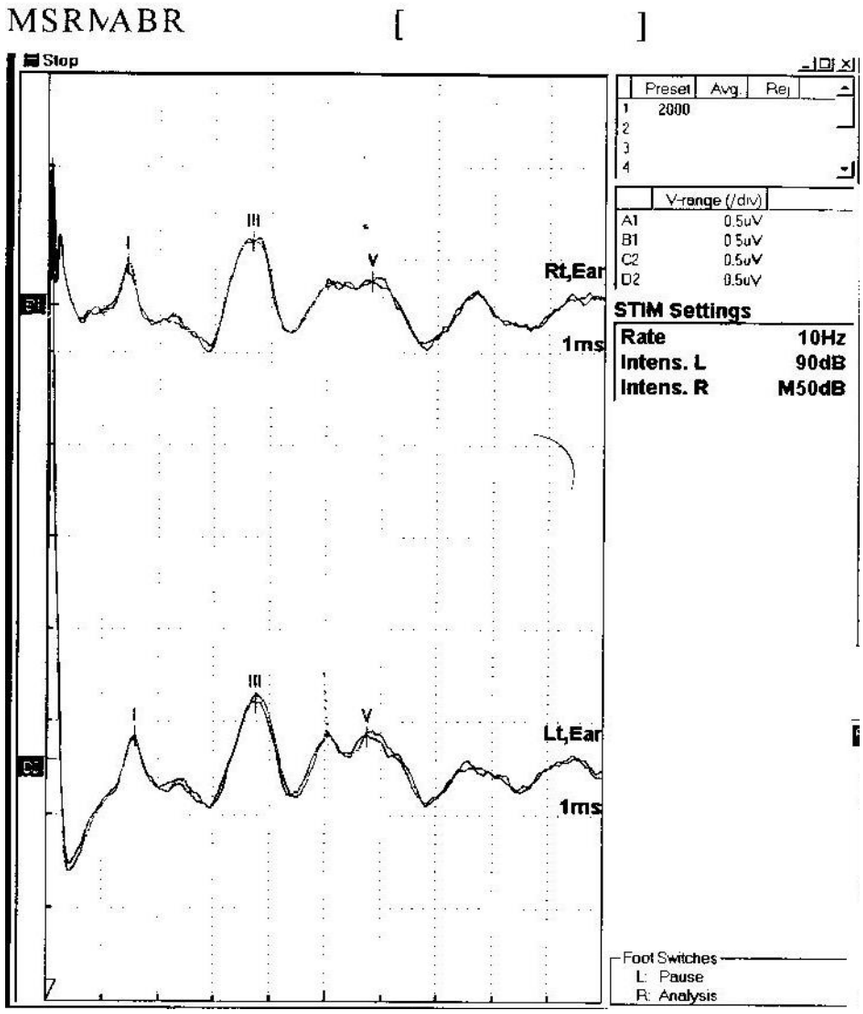

Fig. 1: BAEP waveforms in the full-term infants.

infants and full term infants (P>0.05). (Table-I). This suggests that the peripheral neuronal maturity of the auditory pathway is complete in both the groups.

The mean latency of BAEP waveform V in the preterm infants was 6.18±0.34 ms, 6.11±0.33 ms and in the term infants was 5.92±0.42 ms, 5.88±0.38 ms for the right and left ears respectively (Table-I).

Thus the mean pattern of absolute latency of BAEP waveform V was significantly prolonged in the preterm infants than the full term infants (P<0.05) (Table-I). This is probably suggestive of the neuronal immaturity of the central auditory pathway in preterm infants.

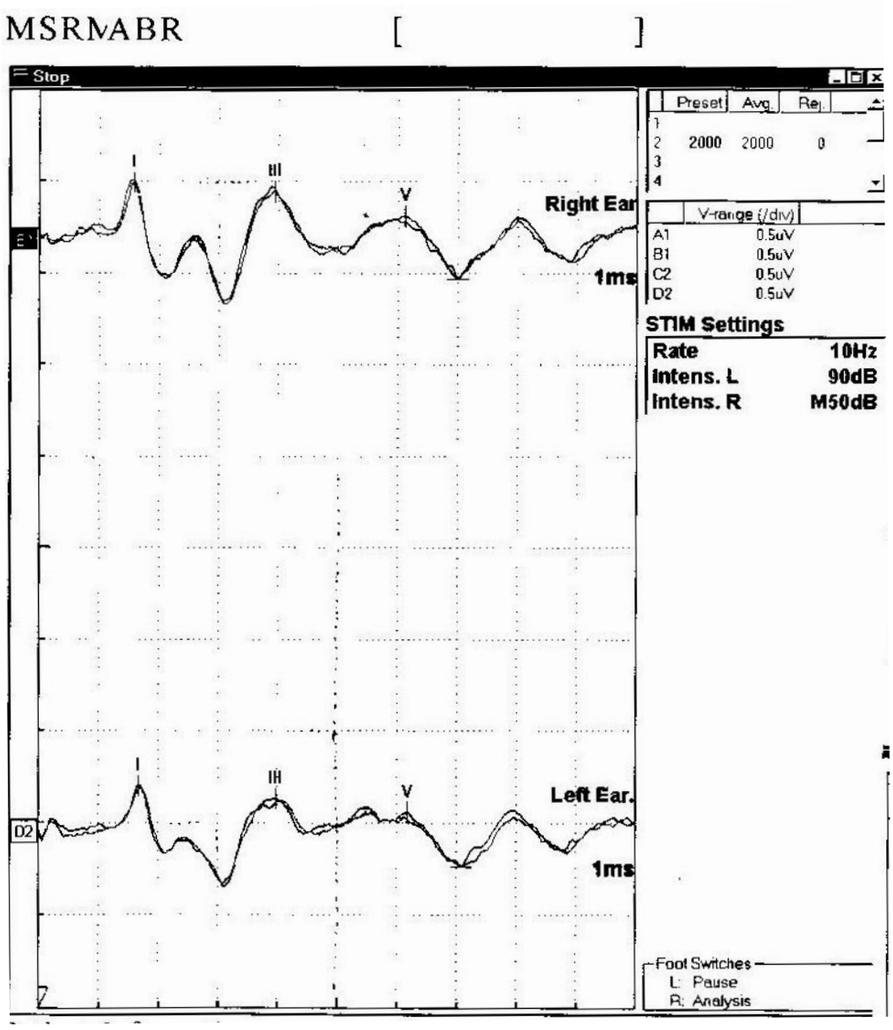

Fig. 2: BAEP waveforms in preterm infants.

The inter-peak latency I-III in the preterm infants was 2.47±0.31 ms, 2.35±0.55 ms and in the term infants was 2.57±0.43 ms, 2.50±0.30 ms for the right and left ears respectively. (Table-II). The inter-peak latency III-V in the preterm infants was 2.22±0.93 ms, 2.27±0.95 ms and in the term infants was 2.13±0.92 ms, 2.09±0.96 ms for the right and left ears respectively. (Table-II). The inter-peak latency I-V in the preterm infants was 4.60±0.36 ms, 4.45±0.98 ms and in the term infants was 4.53±0.48 ms, 4.44±0.32 ms for the right and left ears respectively (Table-II).

Thus the inter-peak latencies - I-III, III-V and I-V did not show significant difference between the two groups (P>0.05) (Table-II)

TABLE I: Comparison of Mean Latency of BAEP waveforms between the Preterm and Full-Term groups.

Latency (ms) (Mean±SD)	*Ear*	*Preterm*	*Full-Term*	*P value*
I	Right	1.45±0.23[a]	1.36±0.34[a]	0.306
	Left	1.40±0.37[a]	1.45±0.20[a]	0.500
III	Right	3.82±0.83[a]	3.83±0.85[a]	0.976
	Left	3.74±0.90[a]	3.82±0.84[a]	0.767
V	Right	6.18±0.34[a]	5.92±0.42[a]	0.020*
	Left	6.11±0.33[a]	5.88±0.38[a]	0.030*

Superscripts

1. Comparison with in each group – Right vs Left
   i. Identical Superscripts (a vs a) are non-significant (P>0.05)
2. Comparison between groups - Preterm vs Full-Term
   i. *denotes significant (P<0.05)

suggesting a comparable nerve conduction velocity.

DISCUSSION

BAEP parameters were recorded and compared in the preterm and the full-term infants. The BAEPs from the right and left ears within the same group were comparable with no significant difference. BAEPs from both ears were recorded to understand if there was any difference in the audiological maturation and function between the two ears.

Routinely a five component BAEP wave is recorded and measured: waves I and II arise from the distal and rostral portions of the eighth nerve, respectively; wave III is from the pons and waves IV and V are from the midbrain. A recognisable BAEP can be recorded in preterm infants of 28-32 weeks in gestational age (8, 15), consisting of a series of three major waves (i.e., I, III, and V). The neural generators for Waves I and III in humans are the auditory nerve and cochlear nucleus, respectively. The generator for Wave V is the termination of the fiber tract of the lateral lemniscus (16). The absolute latencies of BAEP waves and their inter-peak latencies progressively decrease over the course of neurological development (17). The BAEPs undergoes rapid changes and development in the first 4 days of life in a full-term infant (18).

The mean absolute latencies of BAEP waveforms, I and III did not show significant difference between the two groups. The mean absolute latency of BAEP waveform V was significantly prolonged in the preterm infants than the full-term infants. The later component (i.e., Wave V) undergoes more marked changes in latency at full term than the most peripheral components (i.e., Waves I and III). This is due to the earlier maturation of the peripheral nervous system relative to the later maturing central auditory pathways (19). The prolonged latency of the BAEP waveform V in the preterm reflect a probable incomplete neural myelination of the fibers in the auditory pathway, reduced axon diameter, and immaturity in synaptic function (20, 21, 22). This observation reflects a delayed maturation of the central auditory pathway and supports the earlier findings that BAEP waveforms latencies are delayed in preterm infants due to the prematurity itself (2, 10). At the same time, there is no denial of the possibility of experience playing a crucial role in the developmental process (11). There is a probable necessity of a much prolonged period of extra-uterine exposure to the environmental stimuli in the preterm to

exert some effect on the maturation process.

The inter-peak latencies (I-III, III-V and I-V) did not show significant difference between the two groups reflecting a comparable nerve conduction velocity among the two groups.

The myelination of the central auditory pathway follows that of the peripheral auditory pathway. The prolonged latency of BAEP waveform V observed in the present study is probably suggestive of a retarded myelination of the central auditory pathway. This could partially be responsible for the differences found between preterm and full term infants (23).

The major limitation of the study is its cross-sectional nature. A prospective longitudinal study with a larger sample would be beneficial to know about the changes happening and also to study the duration when the preterm brain maturation probably catches up with that of the full term babies. Application of BAEP and other evoked potentials may also be useful in the monitoring the beneficial effects of the treatment modalities in such preterm infants.

Conclusions:

The preterm infants have a prolonged latency of BAEP waveform V suggestive of a retarded myelination of the central auditory pathway. Thus BAEP could be a useful electrophysiological test to assess neuronal myelination and maturation in the preterm infants.

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