Original article:

Auditory Evaluation in High Risk Infants with Hyperbilirubinemia Using Brainstem Evoked Response Audiometry

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Abstract:

Introduction: Neonatal hyperbilirubinemia is one of the most important factors affecting the auditory system and can cause sensorineural hearing loss.This study aim to evaluate the degree of hearing impairment in infants suffering from hyperbilirubinemia by using BERA and to analyse and compare BERA responses in these high risk infants with agematched controls.

Methods: Hundred high risk infants having one or more risk factors attending Pediatric OPD of Bapuji and Chigateri Hospital and thirty age matched controls satisfying the inclusion criteria were randomly selected from immunization centre were subjected to BERA. Parameters such as absolute latencies of waves I, II, III, IV and V, Interpeak latencies I-III, I-V and III-V and amplitude ratio V/I were analysed by using unpaired t-test. Intragroup comparison was made using chi-square test.

Observations and Results: Out of the 100 cases, 48 babies had hyperbilirubinemia. No BERA response was obtained from 12 babies, rest 36 had increased Wave V threshold when compared to control and the difference was significant statistically.Absolute latency (in Ms) of Wave V was prolonged in hyperbilirubinemiagroup when compared to controls.When babies with hyperbilirubinemia were compared with cases associated with other risk factors except hyperbilirubinemia , the absolute latencies (in Ms) of wave I and wave V were significantly increased.

Conclusion: The present study indicates that hyperbilirubinemia contributessignificantly for hearing impairment. Therefore it is essential to screen allthe infants at the earliest, to prevent adverse effect on the developing auditorypathway.

Key words: Brainstem Evoked Response Audiometry (BERA), hearing impairment,high risk infants, hyperbilirubinemia.

Introduction:

A child's normal speech and language development depend on the ability to hear. The prevalence of hearing loss is 0.5-6/1000 neonates across the globe. [1]Neonatal hyperbilirubinemia continues to be a problem, responsible for neonatal morbidity and mortality and Jaundice is one of the most common problems occurring in newborns. [2]Neonatal Hyper bilirubinemia is an adverse perinatal clinical event that places the affected neonate at an increased risk of hearing impairment.[3]

Hyperbilirubinemia during the neonatal period with associated kernicterus has been etiologically tied to Sensorineural hearing loss (SNHL) for decades. Insufficient conjugation of bilirubin, impaired serum albumin binding or enhanced production of unconjugated bilirubin can elevate serum levels sufficiently to permit passage through the Blood Brain Barrier (BBB), with resulting bilirubin deposition in the basal ganglia, including the ventrocochlear nucleus, leading to neurologic sequelae such as SNHL.[4]

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Hearing impairment has a devastating detrimental and invariable adverse impact on the development of children. Late detection causes irreversible stunting of the language development potential of the child.Failure to detect congenital or acquired hearing loss may result in lifelong deficit in speech & language acquisition, poor academic performance, personal-social maladjustment, and emotional difficulties.[5]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.[6]It is not significantly altered by state of consciousness, drugs and variety of environmental factors including other sensory input to the cortex.[7]So the present study evaluate if hyperbilirubinemia is associated with acute auditory neuropathy in high risk infantswithout any comorbid medical conditions and middle ear disease.

Aims & Objectives:

1. To assess the degree of hearing impairment in infants with hyperbilirubinemia by using BERA.
2. To determine the threshold of hearing in infants with hyperbilirubinemia by observing wave'V' at the minimum intensity of click stimulus.
3. To compare the auditory brainstem response in infants with hyperbilirubinemia with age matched controls
   a. Absolute latency of wave I, II, III, IV and V
   b. Interpeak latencies of I-III, I-V and III-V waves
   c. Amplitude ratio of wave V/I

Material and methods:

In this study 100 high risk infants having one or more risk factors, according to the criteria stated by American Academy of Pediatrics, JCIH 2007 were selected from Bapuji Hospital and Chigateri General Hospital, attached to J.J.M. Medical College, Davangere and 30 age matched controls were selected randomly from the immunization centre and pediatric OPD.

Inclusion Criteria:

1. Babies < 1 year
2. Family history of permanent childhood hearing loss
3. Neonatal intensive care of more than 5 days or any of the following regardless of length of stay. Extracorporeal membrane oxygenation (ECMO), assistedventilation, exposure to ototoxic drugs or loop diuretics (furosemide) and hyperbilirubinemia that requires exchange transfusion.
4. In utero infection such as cytomegalovirus, herpes, rubella, syphilis and toxoplasmosis.
5. Craniofacial anomalies
6. Birth weight < 1500g
7. Bacterial meningitis
8. Gestational age < 37 weeks
9. Apgar scores < 4 at 1 minute or < 6 at 5 minutes
10. Normal age matched term babies with birth weight > 2500gm.

Exclusion Criteria:

1. Severe multiple anomalies
2. Incompatible with life
3. Atresia or stenosis of external ear canal
4. Untreated otitis externa
5. Babies more than one year of age.

100 high risk infants and 30 age matched controls satisfying the inclusion criteria were included in the study. Written informed consent was taken from the parents after explaining them the procedure and its significance in their vernacular language. Detailed history and thorough ENT examination was done before the procedure.

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BERA recording:The infants were subjected to BERA testing on RMS EMG EP MARK-IImachine manufactured by the RMS RECORDERS and MEDICARE SYSTEM, CHANDIGARH.

Procedure in brief:

Infants were sedated with syrup Trichlofos (pedichoryl) 20mg/kg body weight. The skin at the point of placement of electrodes were cleaned with 'abrasive strip. Recording of BERA was carried out in a quiet and semi-darkened room. Surface electrodes were placed at the vertex (CZ), both mastoids (Ai and Ac) and forehead (ground). The resistance was kept below 5K. Monoaural auditory stimulus consisting of rarefaction clicks of 100 microseconds were delivered through electrically shielded earphones at the rate of 11.1/sec. Contralateral ear was masked with pure white noise of 40dB. A band pass of 150-3000Hz was used to filter out undesirable frequencies in the surroundings. Responses to 2000 click presentations were averaged.

Parameter studied:

BERA threshold for each ear with absolute latencies of wave I, II, III, IV and V waves interpeak latencies (IPL) of I-III, I-V and III-V and amplitude ratio V/I were considered from the recording for comparison among high risk infants and controls.

Statistical analysis:

The results are expressed as mean and standard deviation. Unpaired t-test was used for intergroup comparisons, p-value of 0.05 or less has considered as statistical significance. Chi-square test for comparing the categorical data.

Observations and Results:

Out of the 100 cases, 48 babies had hyperbilirubinemia. No BERA response was obtained from 12 babies, rest 36 had Wave V threshold of 50.97 + 25.21dB when compared to control 30+0 dB and highly significant statistically (Graph No.9).Absolute latencies (in Ms) of Wave I were 1.79 + 0.28 and 1.68 + 0.20, Wave II 2.79 + 0.39 and 2.67 + 0.27 Wave III 4.32 + 0.64 and 4.24 + 0.26 Wave V 6.76 + 0.91 and 6.33 + 0.35 in hyperbilirubinemia and control group respectively. All these parameters were delayed in hyperpilirubinemia group, however statistically significant delay was seen in wave V latency.

IPL I – III, I-V, III – V and amplitude V/I ratio were slightly higher than the control but not significant statistically (Table No. 1).

Within the case group, when babies with hyperbilirubinemia were compared with cases associated with other risk factors except hyperbilirubinemia , the absolute latencies (in Ms) of wave I were 1.79 + 0.28 and 1.63 + 0.30 and wave V were 6.76 + 0.91 and 6.38 + 0.72 respectively.These values were significantly delayed when compared to the high risk infants without hyperbiliribinemia (Table no. 2).

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Table No -1. Comparison of BERA parameters in Hyperbilirubinemia cases withcontrol group.

Measurement	Controls (N=30)		Hyperbilirubinemia (N= 36)		Hyperbilirubinemia Measurement v/s Controls	
	Mean	SD	Mean	SD	t Value	P Value
V (dB) Threshold	30. 0	0	50.97	25.21	- 5.06	< 0.001 *
I	1.68	0.20	1.79	0.28	-1.64	0.11
II	2.67	0.27	2.79	0.39	-1.42	0.15
III	4.24	0.26	4.32	0.64	-0.56	0.57
IV	5.47	0.48	5.66	0.93	-1.01	0.32
V	6.33	0.35	6.76	0.91	-2.43	<0.05*
I-III	2.56	0.27	2.64	0.5	-0.79	0.43
I-V	4.66	0.35	4.91	0.75	-1.67	0.09
III-V	2.10	0.33	2.2	0.47	-1.6	0.11
V/I	3.60	5.11	3.62	5.87	-1.48	0.14

Unpaired t-test: * Significant ** Highly significant

Table No -2. Comparison of BERA parameters in Hyperbilirubinemia caseswith other high risk infants without jaundice

Measurement	Hyperbilirubinemia +			Hyperbilirubinemia–			Hyperbilirubinemia + v/s hyperbilirubinemia–		
	N	Mean	SD	N	Mean	SD	t Value	p Value	Significance
V (dB) Threshold	36	50.97	25.21	41	50.12	18.08	0.17	0.86	NS
I	36	1.79	0.28	41	1.63	0.30	2.41	<0.05	Sig
II	36	2.79	0.39	41	2.69	0.37	1.15	0.25	NS
III	36	4.32	0.64	41	4.10	0.60	1.55	0.12	NS
IV	36	5.66	0.93	41	5.59	0.70	0.42	0.66	NS
V	36	6.76	0.91	41	6.38	0.72	2.04	<0.05	Sig
I-III	36	2.64	0.50	41	2.47	0.52	1.46	0.14	NS
I-V	36	4.92	0.75	41	4.81	0.66	0.68	0.50	NS
III-V	36	2.20	0.47	41	2.35	0.61 -	-1.18	0.24	NS
V/I	36	3.62	5.87	41	4.67	4.97 -	-0.84	0.40	NS

Unpaired t – test: NS - Non Significant, Sig-Significant

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Table No- 3. BERA grading in relation to hyperbilirubinemia.

Hyperbilirubinemia		BERA Grading					Total
		Normal	Mild	Moderate	Severe	Profound	
+	No.	15	10	1	2	8	36
	%	41.7%	27.8%	2.8%	5.6%	22.2%	100%
–	No.	12	15	3	10	1	41
	%	29.3%	36.6%	7.3%	24.4%	2.4%	100%
Total	No.	27	25	4	12	9	77
	%	35.1%	32.5%	5.2%	15.6%	11.7%	100 %

Chi-square	df	P value
12.84	4	0.012

$P < 0.05$, Sig

Discussion:

Hearing loss has a detrimental effect not only on the child's ability to speak and learn the language but also communication ability. Hence, early detection and intervention is the key to normal speech and language development. Interventions can vary from sign language to cochlear implantation.

Brainstem evoked response audiometry though more time-consuming, is an accurate test for early detection of neural conduction irregularities in the auditory pathway. It is a short latency response. It detects electrical activity from the inner ear to the inferior colliculus. It can be reliably recorded even in premature infants of 30 weeks gestational age. It gives an estimate of degree and type of hearing impairment. It helps to find the cause of delayed speech. It is used to localize the site of lesion in patients with hearing loss and vertigo. BERA is superior to pure tone audiometry in malingering patients. Threshold estimation by BERA is used to identify hearing impairment in neonates thus facilitating early rehabilitation. The existence of peak V is considered as sound stimulus perceived by the ear. Pure tone threshold can be obtained by subtracting 5-10 dB from the point where wave V is just identifiable.

Elevated levels of bilirubin are considered toxic for the auditory pathways and the central nervous system, and are included among risk factors for neonatal deafness and encephalopathies. Since BERA wave changes have been associated with hyperbilirubinemia in newborn, BERA monitoring of jaundiced infants may be an important clinical tool for detecting early reversible bilirubin injury. Incidence of hearing impairment in hyperbilirubinemia cases was 58.3%, most common being mild hearing loss which is comparable to Agarwal[8] and Hans Raj[9] but higher than others[10,11].

Prolonged absolute latency of Wave V in our study is in consonance to findings of other authors. Interwave latencies being on the higher side, however was not statistically significant unlike other studies[12, 13, 14]. Significant correlation does exists between total serum bilirubin level and brainstem conduction time[10, 14]. Most of the previous workers have shown the transient nature of bilirubin encephalopathy with

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reversal of changes in almost all patients after therapy[8, 13, 14].

Bilirubin can deleteriously affect the auditory pathway anywhere along its course in the brainstem although the cochlear nucleus is usually most involved leading on to hearing impairment.[15,16] Improved brain functions after phototherapy and /or exchange transfusion may be due to removal of bilirubin from brainstem.

Dorothy et al[17] found the sensitivity of BAEP as a screening test to be 100%, specificity of the test is 86%. With further experience& technologic advances, BAEP may prove justified for wide-spread clinical utilization in the hearing screening of high – risk newborns.

No child is too young for hearing evaluation. Screening programme should be performed in the nursery and well baby clinic during immunization in the first year or better in the first 6 months of age to avoid harmful effect on speech and language development. But surprisingly, no dedicated national programme has been carried out so far in India, for early detection of hearing loss in infants. Neonatal screening can yield high returns. More over screening programme is cost effective as the child who receives early interventions for hearing loss requires less of expensive special education later. The true value of screening may lie in identification of mild to moderate hearing losses that are amenable to treatment and if untreated may manifest like a severe impairment. High risk infants have substantially higher incidence of hearing. So at least all high risk infants must be screened for hearing impairment prior to discharge from hospital using BERA. Retesting of infants with abnormal initial ABR within 3 months and several times within the first year if abnormal responses persists, is important.

Conclusion:

Our finding of a high incidence of hearing loss among infants with severe jaundice is of great public health significance. All the high risk infants with and without severe hyperbilirubinemia should have comprehensive auditory evaluation performed before discharge from the hospital to identify infants with auditory neuropathy. Early identification and intervention is the most important factor in minimizing the impact of hearing loss on a child's development and educational achievements.

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References:

1. Burke MJ, Shenton RC, Taylor MJ. The economics of screening infants at risk of hearing impairment: An international analysis. Int J PediatrOtorhinolaryngol 2012;76:212-8.

2. Sharma R, Grover N. Auditory Brain Stem Responses in Neonatal Hyperbilirubinemia and Effect of Therapy; Indian Journal of Otolaryngology and Head and Neck Surgery. 2006;58(4).
3. Pramodh Sharma, N. P. Chhangani, Kesh Ram Meena, RakeshJora, Navratan Sharma, B. D. Gupta. Brainstem Evoked Response Audiometry (BAER) in neonates with hyper bilirubinemia. Indian Journal of Pediatrics, 2006;73:413-416.
4. Bluestone CD, Stool SE, Alper CM, Arjmand EM, Casselbrant ML, Dohar JE et al. ear and Related structures In : Pediatric otolaryngology. 4th ed. Saunders : Elsevier ; 2003, p.779 – 807.
5. Kumar A, Dhanda R. The identification and management of deaf children. Indian J Pediatr.1997; 64:785-792.
6. Deorari AK, Garg R, Bisht MS, Ahuja GK,Paul VK, Singh M. Auditory brainstemevoked response in normal neonates andinfants. Indian Pediatr 1989;26: 981-986.
7. Wood S Marcormick B, Marson S. Auditory brainstem response in pediatric audiology. Arch Dis Child 1988;63:565-567.
8. Agarwal VK, Shukla R, Misra PK, Kapoor RK, Malik GK. Brainstem auditoryevoked response in newborns with hyperbilirubinemia. Indian Pediatrics.1998;35:513-18.
9. Gupta AK, Anand NK, Raj H. Evaluation of risk factors for hearing impairment in at risk neonates by brainstem evoked response audiometry. Indian J Pediatrics. 1991;58:849 – 55.
10. Boo NY, Rohan AJ, Asma A. Detection of sensorineural hearing loss using automated auditory brainstem evoked response and transient – evoked otoacoustic emission in term neonates with severe hyperbilirubinaemia. Singapore Med I. 2008;49 (3):209 – 14.
11. Ahlfors CE, Parker AE. Unbound Bilirubin concentration i.e. associated with abnormal automated audiotry brainstem response for jaundiced newborns. J Pediatrics 2008:121:976 – 78.
12. Silva DPC, Martim RHG. Analysis of transient otoacoustic emissions and brainstem evoked auditory potentials in neonates with hyperbilirubinemia. Braz J otorhinolaryngol. 2009;75(3):381-86.
13. Sharma R, Grover N, Shankhyan N, Sharma ML. Auditory brainstem responses in neonatal hyperbilirubinemia and effect of therapy. Indian J otolaryngol Head Neck surgery. 2006;58(4):340 – 42.
14. Sharma P, Chhangani NP, Meena KR, Jora R, Shrama N, Gupta BD. Brainstem evoked response audiometry in neonates with hyperbilirubinemia. Indian J Pediatrics. 2006;73(5):413 – 16.
15. Chisin R, Perlman M, Sohmer H: Cochlear and brainstem re responses in hearing loss following neonatal hyper bilirubinemia. Ann OtolRhinol Laryngol.1979;88:352.
16. Perlman M, FainmesserP, Sohmer H, Tamari H, Wax Y, Pevsmer B: Auditory nerve –brainstem evoked responses In hyper bilirubinemic neonates. Pediatr.1983;72:658.
17. Dorothy A. Shannon, PhD, Jacob K. Felix, MD, FAAP, Allan Krumholz, MD, Phillip J. Goldstein, MD, and Kenneth C. Harris Hearing screening of High –Risk Newborns with Brainstem auditory Evoked potentials: A follow –up study. Pediatr.1984;78:92-96.