Original research article

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EXPLORATION OF EARLY AUDITORY EFFECTS OF HYPERBILIRUBINEMIA IN NEONATES USING BERA

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ABSTRACT

Objectives: This study was planned to assess the hearing of infants with Hyperbilirubinemia using brainstem evoked response audiometry (BERA) and to find a possible co-relation between the level of hyperbilirubinemia & the degree of hearing loss. **Methods:** The present study is conducted on 100 neonates to compare their BERA findings on cases presenting with hyperbilirubinemia born and admitted to the NICU of Mahatma Gandhi Medical College & Hospital, Jaipur with 60 control neonates born in MGMCH with no medical and surgical ailment. A detailed history was taken and relevant investigations were done to rule out any other cause of hearing loss. Patients with coexisting causes for hearing loss were excluded from the study. The cases were subject to phototherapy or double volume exchange transfusion. BERA was carried out on the babies atleast 2 months after discharge from the hospital. **Results:** The Mean values for hyperbilirubinemia group were found to be more than the control group. It was found that the mean for the absolute latency of wave V & the
interwave latency of I-V for the 0-12 months age group with bilirubin levels less than 15mg/dL was statistically significant when compared to the group with bilirubin level more than 15mg/dL with a p value of 0.01 & 0.05 respectively. **Conclusion:** Hyperbilirubinemia does have an adverse effect on neonatal hearing which was reflected by BERA parameters of our study.

Key words: Hyperbilirubinemia, BERA, Phototherapy, Exchange transfusion.

INTRODUCTION

Neonatal Hyperbilirubinemia is a well known undesirable perinatal clinical complication that can increase risk of hearing impairment in the affected neonate.**(1)** 70% of term and 80% of preterm neonates during the 1st week of life commonly present with Jaundice. **(2)** Clinico-pathological studies have suggested that bilirubin encephalopathy affects superior olive, lateral leminiscus and inferior colliculus. However, objective methods to identify early CNS involvement of bilirubin toxicity are not easily available. **(3)** An essential aim is the early diagnosis of infants with deep jaundice or impaired hearing so that rehabilitation can be

initiated when the brain is sensitive to development of speech and language. A number of methods have been evaluated to search for a reliable and effective technique for determining auditory functions in the neonates. Brainstem Evoked Response Audiometry (BERA) has explored the possibility of objective testing of hearing functions. It is an easy, effective and noninvasive means of evaluating the functional status of the auditory nerve and the brain stem auditory sensory pathway. It is a simple technique and requires less cooperation of the patient and measures the specific part of the auditory pathway.**(4)** It is not significantly altered by the state of consciousness, drugs and environmental factors like the sensory input to the cortex.**(5)** Timely recourse to effective phototherapy and exchange transfusion may reverse the changes in BERA. The study was thus undertaken to study the initial BERA recordings in icteric term neonates and note its correlation with serum bilirubin levels.

The variations in BERA 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.

METHOD

Study Design:

This is a comparative study conducted on 100 patients & 60 controls.

Settings:

NICU of Mahatma Gandhi Medical College & Hospital, Jaipur.

Source of Data:

100 patients admitted to NICU of Mahatma Gandhi Medical College & Hospital, Jaipur from 1st of January 2013 to 31st May 2014.

Method of Collection of data:

This was a comparative study in which patients were studied in two groups. One group comprised of babies with Hyperbilirubinemia admitted to the NICU & receiving phototherapy or Exchange transfusion and the other group comprised of normal babies with no history of NICU admission or hyperbilirubinemia. All patients were subjected to BERA after a minimum of 2 months after being discharged from the hospital. In each patient of the study group, detailed history was taken and investigations like haemoglobin, total count, differential count, blood sugar, Total serum bilirubin were done. Care was taken to keep into consideration the exclusion criteria through relevant investigations.

Preparation of the patient was done prior to subjecting the patient for a BERA. The same protocol was followed in every case. In all the recruited patients the parts were prepared for the application of the electrodes over the scalp. The baby was given syrup chloral hydrate 20mg/kg body weight. 30 dB to 100 dB rare click stimuli were then delivered to both ears separately & monoaural responses were recorded & analyzed.

Hyperbilirubinemia group:

This group comprised of 100 patients with hyperbilirubinemia admitted to the NICU for phototherapy or exchange transfusion.

Control Group:

In this group, we included of 60 cases with no abnormality & no history of NICU admission; taken from the OPD of Mahatma Gandhi Medical College & Hospital, Jaipur. These patients had come to the OPD for follow up after delivery. These patients were subjected to a BERA after ruling out the presence of any risk

factors for hearing loss & the findings documented. The results of the control group were then used as a comparative scale to interpret the BERA values of the hyperbilirubinemia group.
The following BERA parameters were taken into consideration:-
1. Absolute latency wave V
2. Interwave latency between wave I & III
3. Interwave latency between wave III & V
4. Interwave latency between I & V

An account of-
1. Age.
2. Bilirubin level.
3.Whether patient received phototherapy or exchange transfusion or both was recorded.

Inclusion Criteria
Infants with hyperbilirubinemia requiring treatment in the form of phototherapy or exchange transfusion in the NICU were included in the study as cases.

Exclusion criteria:
1. Neonates born with birth asphyxia
2. Amino glycoside administered patients
3. Patients with Craniofacial malformations
4. Syndromic causes of deafness
5. All causes of conductive deafness
6. A family history of deafness.

Method of statistical analysis: Results were expressed as mean & standard deviation for each of the sub groups.The student 't' test was used to determine whether there was a statistical difference between male and female subjects in the parameters measured. P value < 0.05 was taken as statistically significant.

RESULTS

Age distribution of control & study population:
The control population was divided into 3 groups based on their age i.e. 3-6 months, 6-9 months & 9-12 months. 20 cases were chosen in each age group. These controls were all healthy & normal with no history of hyperbilirubinemia or NICU admission or hearing loss of any kind.

The mean absolute latency & the interwave latencies were calculated along with the standard deviation for each age group correspondingly. These calculations were carried out for varying stimulus intensity levels. An interval was then created in order to compare the data of the cases with the controls. Mean $\pm$ 2 standard deviation was considered as a safe range. Values falling within this range were considered to be within normal limits, whereas values falling out of this interval were considered as abnormal.

3 – 6 Months Age Group:

In this group, maximum Bilirubin was 20.6 mg/dl and minimum was 7.9 mg/dl with a mean value of 14.2mg/dl. Of the total 45 cases in this group, 25 cases had Bilirubin Level > 15 mg/dl & rest 20 have < 15 mg/dl. Recordable BERA waves were obtained in 7 of 25 cases with Bilirubin Level > 15 mg/dl & 14 of 20 cases with Bilirubin Level < 15 mg/dl.

DISCUSSION

Elevated serum levels of unconjugated bilirubin are considered toxic for the auditory pathways and the central nervous system, and are included

among the risk factors for neonatal deafness and encephalopathies. **(6)** A high concentration of biliary pigments is immediately managed with phototherapy and/or exchange transfusion; the exchange transfusion is applied for severe cases and those are not responding to phototherapy.**(7)** The results of the present study showed that higher serum bilirubin levels did alter BAEP electrophysiological potential latencies. Some authors like Lenhardt et al have showed a cause-effect relation between these variables.**(8)**

The values of the absolute latency of wave V & interwave latencies were seen to progressively reduce as the age increased which is consistent with studies conducted by Ottaviani et al and Maurizi et al .**(9,10)**

When compared to the control group, the values of the hyperbilirubinemia group were increased for all the 3 interwave latencies. When compared within the hyperbilirubinemia group, the values of all the interwave latencies in the group with TSB levels greater than 15mg/dL were higher than those of the group with TSB values less than 15mg/dL. These findings are consistent with those of Lenhardt et al. & Nakamura et al. **(8, 11)** where in a cause effect relationship had been demonstrated between the bilirubin levels & the ABR findings. However, some studies such as those of Daniela Polo Camargo da Silva et al do not show a cause effect relation between ABR findings & bilirubin levels. **(12)** The reversibility of auditory pathway damage following the treatment of hyperbilirubinemia could not be established in this study due to delays in referring these children. However, auditory pathway alterations were recorded at two months post-therapy, which recommended temporary or permanent auditory sequelae. Thus it is important to follow up these children on an ambulatory basis, monitoring not only language, but also cognitive development.

CONCLUSION

Hyperbilirubinemia does have an adverse effect on neonatal hearing, which was reflected on the BERA parameters of our study.

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Conflict of interest: None declared

Ethical approval: The study was approved by the institutional ethics committee

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Table 1:Age Distribution (Control population)

AGE	3-6 months	6-9 months	9-12 months	Total
No. of Cases	20	20	20	60
Mean Age	4.25	7.45	10.50	

Table 2 : Age Distribution (Study Population)

AGE	3-6 months	6-9 months	9-12 months	Total
No. of Cases	38	31	31	100
Mean Age	4.65	7.91	11.09	

Table 3 : Mean Absolute Latency of Wave V & Standard Deviation of Control Population (3-6 months)

Db Level	30dB	40dB	50dB	60dB	70dB	80dB	90dB	100dB
Average (mS)	7.79	7.41	7.56	6.79	6.31	6.25	5.55	5.09
Std Dev	0.25	0.24	0.26	0.23	0.20	0.20	0.17	0.17

Table 4 : Mean Absolute Latency of Wave V & Standard Deviation of Control Population (6-9 months)

Db Level	30dB	40dB	50dB	60dB	70dB	80dB	90dB	100dB
Average (mS)	11.5	7.29	6.95	6.71	6.31	6.12	5.85	5.49
Std Dev	0.10	0.25	0.26	0.23	0.19	0.20	0.17	0.17

Table 5 : Mean Absolute Latency of Wave V & Standard Deviation of Control Population (6-9 months)

Db Level	30dB	40dB	50dB	60dB	70dB	80dB	90dB	100dB
Average (mS)	7.55	7.09	6.65	6.31	6.11	5.92	5.75	5.49
Std Dev	0.10	0.25	0.26	0.23	0.19	0.18	0.09	0.17

Table 6 : Mean Inter Wave Latencies & Standard Deviation of Control Population (3-6 months)

IWL	I-III	III-V	I-V
Average (mS)	2.57	2.19	4.71
Std Dev	0.16	0.17	0.26

Table 7 : Mean Inter Wave Latencies & Standard Deviation of Control Population (6-9 months)

IWL	I-III	III-V	I-V
Average (mS)	2.37	2.09	4.41
Std Dev	0.14	0.17	0.16

Table 8 : Mean Inter Wave Latencies & Standard Deviation of Control Population (6-9 months)

IWL	I-III	III-V	I-V
Average (mS)	2.27	2.06	4.31
Std Dev	0.14	0.14	0.18

Table 9: Showing No. of Cases with Increased Inter Wave Latencies in both Study groups with respect to Rt. & Lt. Ear in age group of 3-6 Months

INTER WAVE LATENCIES	**STUDY 1 (>15 mg/dl)**		**STUDY 2 (<15 mg/dl)**	
	Rt.Ear	Lt. Ear	Rt.Ear	Lt.Ear
I-III	3	2	5	6
III-V	2	3	5	5
I-V	5	2	6	4

Table 10: Showing Mean Inter Wave Latencies (IWL) in both Study & Control groups with respect to Rt. & Lt. Ear in age group of 3-6 Months

MEAN INTER WAVE LATENCIES(in milliseconds)	STUDY 1 (>15 mg/dl)		STUDY 2 (<15 mg/dl)		CONTROL
	Rt. Ear (SD)	Lt. Ear (SD)	Rt. Ear (SD)	Lt. Ear (SD)	
I-III	2.76 (1.03)	2.54 (0.46)	2.77 (0.86)	2.60 (0.74)	2.59 (0.14)
III-V	2.61 (0.70)	2.49 (0.92)	2.63 (1.12)	2.33 (0.85)	2.24 (0.15)
I-V	5.41 (0.69)	5.18 (0.77)	5.27 (1.07)	4.87 (1.02)	4.66 (0.24)

6 – 9 Months Age Group:

Table 11: Showing No. of Cases with Increased Inter Wave Latencies in both Study groups with respect to Rt. & Lt. Ear in age group of 6-9 Months

INTER WAVE LATENCIES	STUDY 1 (>15 mg/dl)		STUDY 2 (<15 mg/dl)	
	Rt.Ear	Lt. Ear	Rt.Ear	Lt.Ear
I-III	5	3	2	3
III-V	4	5	4	4
I-V	3	5	6	2

Table 12: Showing Mean Inter Wave Latencies (IWL) in both Study & Control groups with respect to Rt. & Lt. Ear in age group 6-9 Months

MEAN INTER WAVE LATENCIES(in milliseconds)	STUDY 1 (>15 mg/dl)		STUDY 2 (<15 mg/dl)		CONTROL
	Rt. Ear (SD)	Lt. Ear (SD)	Rt. Ear (SD)	Lt. Ear (SD)	
I-III	2.57 (1.03)	2.86 (0.84)	2.19 (0.63)	2.53 (0.97)	2.39 (0.12)
III-V	2.84 (0.87)	2.42 (0.65)	3.16 (1.07)	2.56 (0.71)	2.04 (0.15)
I-V	5.46 (1.05)	5.29 (0.88)	5.26 (0.96)	5.04 (1.00)	4.53 (0.17)

9 – 12 Months Age Group:

Table 13: Showing No. of Cases with Increased Inter Wave Latencies in both Study groups with respect to Rt. & Lt. Ear in age group of 9-12 Months

INTER WAVE LATENCIES	**STUDY 1 (>15 mg/dl)**		**STUDY 2 (<15 mg/dl)**	
	Rt.Ear	Lt. Ear	Rt.Ear	Lt.Ear
I-III	1	0	6	6
III-V	2	2	7	9
I-V	2	1	10	9

Table 14: Showing Mean Inter Wave Latencies (IWL) in both Study & Control groups with respect to Rt. & Lt. Ear in age group of 9-12 Months

MEAN INTER WAVE LATENCIES(in milliseconds)	**STUDY 1 (>15 mg/dl)**		**STUDY 2 (<15 mg/dl)**		**CONTROL**
	Rt. Ear (SD)	Lt. Ear (SD)	Rt. Ear (SD)	Lt.Ear (SD)	
I-III	2.86 (0.62)	2.98 (0.17)	2.93 (0.89)	2.60 (0.67)	2.29 (0.15)
III-V	2.22 (0.63)	2.56 (0.70)	2.68 (0.69)	3.03 (1.37)	2.01 (0.12)
I-V	4.31 (0.90)	4.57 (0.77)	5.60 (0.67)	5.72 (1.06)	4.20 (0.19)

Nature of Treatment Modality Opted: Table 15

	PHOTOTHERAPY	DOUBLE VOLUME EXCHANGE TRANSFUSION
3 – 6 months	**38**	**9**
6 – 9 months	**31**	**5**
9 – 12 months	**31**	**3**
Total	**100**	**17**

Table 16: Total Serum Bilirubin Levels in the Study population

BILIRUBIN LEVELS	>15 mg/dl	<15 mg/dl	Total
No. Of Cases	**45**	**55**	**100**

Out of 45 cases with Bilirubin > 15 mg/dl, 25 have no recordable waves on BERA.

Table 17: Hearing Threholds in the Study Population Lt. Ear

Threshold	30dB	40dB	50dB	70dB	80dB	90dB	100dB	110dB	No Response	Total
No. of cases	11	2	16	9	1	7	2	3	49	100

Table 18: Hearing Threholds in the Study Population Rt. Ear

Threshold	30dB	40dB	50dB	70dB	80dB	90dB	100dB	110dB	No Response	Total
No. of cases	7	3	11	12	3	8	5	2	49	100