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Original Research Article

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Brainstem Evoked Auditory Responses in Neonatal Hyperbilirubinemia Infants

Dr. Bhagya V*[1] Dr. Manjushree P[2] and Dr. Guruprasad D[3]

[1]*Professor of Physiology, JJMMC, Davangere, India*

[2]*Postgraduate in Physiology, JJMMC, Davangere, india*

[3]*Professor of Neonatology, JJMMC, Davangere, india*

Abstract: Jaundice is a common finding in neonates affecting 70% of term and 80% of preterm neonates during the first week of life. Objective of this study is to evaluate auditory and brainstem responses in hyperbilirubinemia infants and to see if there is any statistically significant increase in latencies of wave I and V waves with rise in bilirubin levels. In the present study we have taken 53 infants with hyperbilirubinemia>11mg% & with no other risk factors like preterm, low birth weight, birth asphyxia and age and sex matched controls who visited pediatric OPD of Bapuji Child Health Centre were evaluated using RMS EMG. EP MARK –II machine. Latencies of Waves I and V and inter-peak latency of I-V were recorded. Latency of wave V and IPL I-V were increased slightly compared to normal control subjects. Increase in the threshold leading to hearing impairment in the affected infants and complete deafness where none of the waves were recorded signify that hyperbilirubinemia is a risk factor for deafness. Since hyperbilirubinemia is a risk factor for hearing impairment, their hearing screening by BERA at the earliest and follow up will help in their earliest initiation of rehabilitation when the brain is sensitive to the development of speech & language.

Keywords: Hyperbilirubinemia; wave V; brainstem responses; risk factor

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***Corresponding Author**

Dr. Bhagya V , Professor of Physiology, JJMMC, Davangere,India

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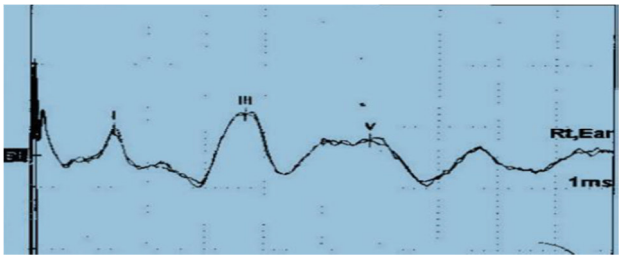
1. INTRODUCTION

Jaundice is a common finding in neonates affecting 70% term and 80% of preterm neonates during the 1st week of life. Hyperbilirubinemia during the neonatal period is an important risk factor for neonatal auditory impairment.[1-3] After delivery of the fetus and entrance to a new environment; neonate encounters a critical situation with increased oxygen concentration and increased production of bilirubin.[4] If indirect bilirubin is increased it can cross blood-brain barrier and precipitate in different parts of nervous system, such as basal ganglia, brainstem, cerebellum and hippocampus. Although most infantile hyperbilirubinemia (60%) are physiologic and harmless[5], their effect on hearing has to be detected earlier. Even short-term increases in bilirubin level can induce temporary or permanent changes in evoked potentials such as increase in threshold and wave latency (I-V) in ABR (auditory brainstem responses), which shows sensitivity of both peripheral and central auditory systems to bilirubin.[5] Hearing impairment is one of the most important causes of speech problems in children. If the diagnosis and treatment of hearing impairment is delayed, it could cause developmental, emotional, and social problems for the child and their family. To initiate rehabilitative procedures as early in life as possible a screening method to detect auditory disabilities in hyperbilirubinemia infants is of great importance. Deafness in the 1st three years of life may impair the full development & maturation of the auditory system and it is well known that deafness in infancy and childhood interferes with normal development of speech and language. In the absence of normal speech, child's ability to communicate is restricted and this has a negative impact on child's social, emotional, cognitive and academic development.[6] Consequently, as a child grows into adulthood, his/her vocational and academic potential is significantly attenuated and family/society is left to bear the cost of the care of an otherwise healthy individual for life. To prevent this and to initiate rehabilitative procedures as early in life as possible a screening method to detect auditory disabilities in newborns is of great importance. Although many methods like -behavioral audiometry, impedance audiometry, respiratory and cardiac responses and crib movement systems are evaluated, Brainstem evoked response audiometry (BERA) which yields information on threshold sensitivity of peripheral part of auditory apparatus and on conduction velocity in brainstem[6] is the satisfactory procedure which can be performed with ease in children. In our previous studies[7] we observed an increase in latency of wave I,V and I-V inter-peak latency in hyperbilirubinemic infants, but a correlation to bilirubin levels will give us more useful data to analyze the toxic effects of bilirubin on hearing. In addition, not many studies are there on brainstem evoked responses correlating bilirubin levels. Hence, the present study is done to know the incidence of hearing loss in neonatal hyper bilirubinemia infants, to evaluate the waves I, V and IPL I-V at different bilirubin levels.

2. MATERIALS AND METHODS

53 Infants with hyper bilirubinemia(>11mg%) with no other risk factors like preterm, low birth weight, birth asphyxia, age and sex matched controls who visited pediatric OPD of Bapuji Child Health Centre, JJM Medical college, Davangere, Karnataka state, India were selected for the study. Institutional Ethical committee approval with reference no. 02-ERBC-STP/14-15 was taken to conduct the study. And an informed written consent was taken from all the patient's parents. All patients were subjected to the test procedures with prior appointment. An ENT check-up was done to rule out the possibility of wax, ear infection, middle ear problems etc. The parents' were instructed to wash the scalp of the child thoroughly as a requirement of the test. Prior to the test, each child was examined by the pediatrician and the dosage for sedation was prescribed. Drug used for sedation was syrup Triclofos 20mg/kg body wt. The instrument used was RMS EMG. EP MARK –II machine, fully computerized, manufactured by RMS RECORDERS & MEDICARE SYSTEM Chandigarh. Test was carried out in a pre–cooled, quiet, dimly lit room with the subject relaxed in supine position with eyes closed. The skin was cleaned with spirit and OMEN abrasive skin preparatory paste. The silver electrodes were placed as follows: Cz–vertex, both mastoid, (Ai and Ac) forehead (ground). Resistance was not more than 1ohm. Electrode electrolyte gel was used and electrodes were fixed. Acoustically shielded THD 32 ear phones were placed on the ear and head bands were adjusted. Monaural auditory stimuli consisting of rarefaction clicks of 100 microseconds with intensities starting from 30 dB to 100 dB were delivered through electrically shielded earphones at a rate of 11.1/sec. Contra-lateral ear was masked. The filter settings used were 150 Hz–3000Hz. The polarity used was alternate and the analysis time was 10m/sec. About 2,000 responses were averaged. Latencies of Waves I, III & V and inter peak latency of I-V were recorded. The existence of peak V was considered as a sound stimulus heard and perceived by the auditory mechanism. The threshold for each ear was confirmed. A normal recording of waveforms is shown in the figure 1



The guidelines used for the confirmation of peak V were as follows:
1. Peak V occurs around latency of 5.7 m/sec with S.D. of 0.25 (as per our norms).
2. With decrease, an intensity level latency of peak V increases and its amplitude decreases.
3. Peculiar in shape.
Normal latency of wave I for infants is 1.47+/-0.19, of wave V is 6.06+/-0.26, and IPL I-V is 4.58+/-0.24[8]

Fig.1 Normal recording of waveforms

3. STATISTICAL ANALYSIS

SPSS Version 20 for windows package was used to analyze the data. Out of 53 infants, in two cases we were not able to record any waves even at 100dB in both the ears, in two other cases not able to record any waves in one ear signifying severely affected ear. The latencies we got from the recording made in the left out 100 ears from the other infants are shown in the table number 1. Depending on the serum bilirubin levels 3 groups were made.

Table 1. Comparison of latencies at different bilirubin levels

Wave atency	Case Group – Serum Bilirubin-mg/dl			
	Normal	11-15	16-20	>20
I	1.76 ±0.3	1.67±0.1	1.7±0.2	1.6±0.2
V	6.3±0.2	6.2±0.3	6.1±0.4	6.3±0.5
Intervals I-V	4.5±0.3	4.5±0.4	4.4±0.4	4.7±0.6

From the table 1, we can observe that not much of a difference is seen in wave I latency. Though the increase in wave V latency was not statistically significant with p>0.01, Wave V latency was increased to a little extent with bilirubin levels above 20 mg /dl. And there was an increase in the threshold of wave recording with raised bilirubin levels above 15 mg /dl.±SD

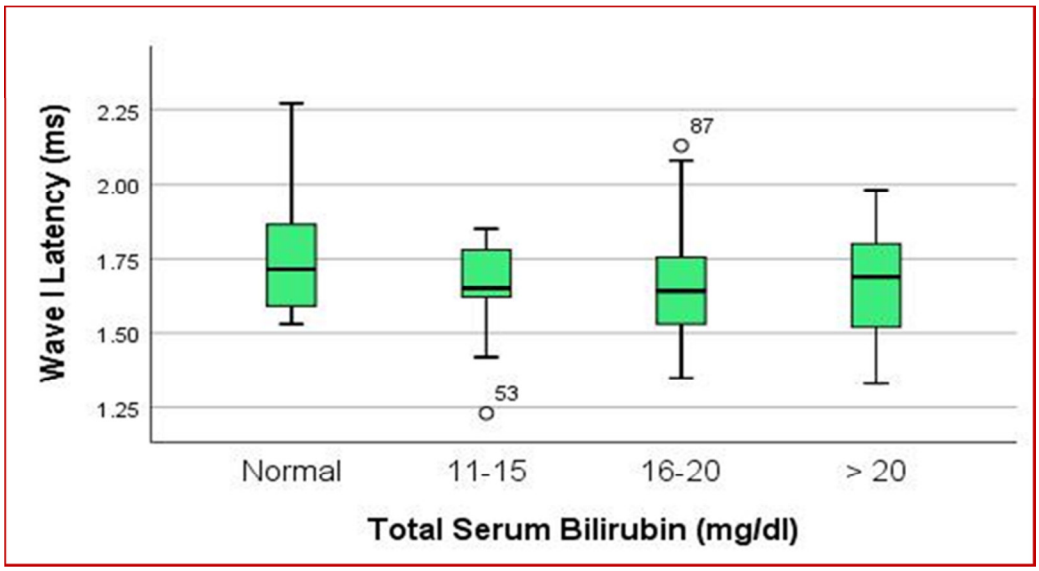


Fig.2 comparison of wave I latencies

We can observe from fig. 2, wave I latency was not raised compared to the normal control groups.

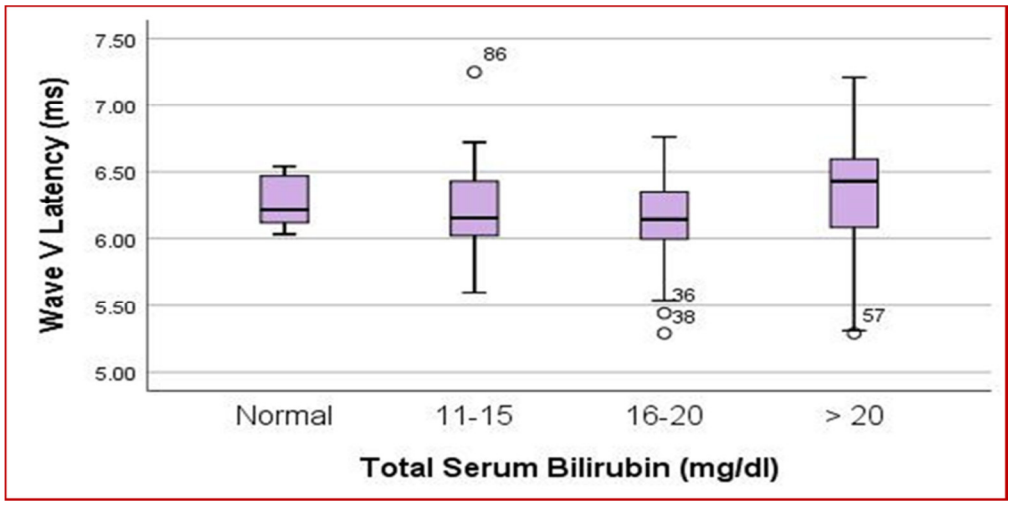


Fig. 3 comparison of wave V latencies

Even though there was no significant increase in wave V latency with rise in bilirubin levels as seen in fig. 3 but the threshold was increased signifying the neurotoxicity of bilirubin.

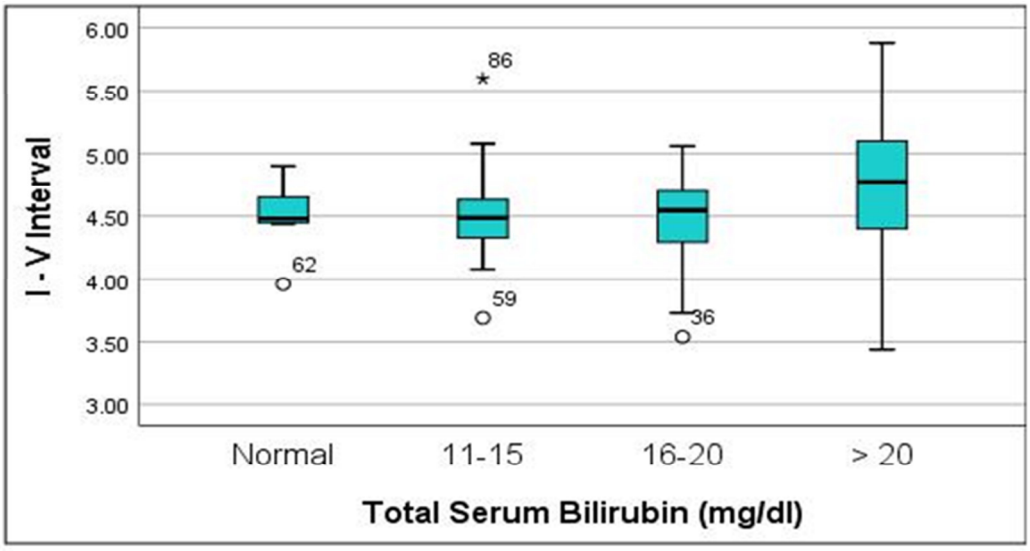


Fig. 4 comparison of I-V inter-peak latencies

As seen in fig. 4, there was an increase in I-V inter-peak latency indicating delay in conduction from cochlear nerve to brainstem. As per their requirement, cases were sent for further rehabilitative procedures. High risk neonates should undergo screening for hearing impairment.[9]

4. DISCUSSION

Hyperbilirubinemia is one of the most important problems during the infantile period. In its severe form, it affects the brain and causes kernicterus. This disease is caused due to precipitation of bilirubin in nervous tissues. Bilirubin is known to inhibit mitochondrial enzymes and affect DNA synthesis and ion exchange. It not only disturbs neuro-excitatory signals, impairs nerve conduction also. [1,10] Basal ganglia, various nuclei in the brainstem, cerebellum and hippocampus being the most affected organs. As a result of the damage to these organs, those patients will have cerebral palsy, mental retardation and sensorineural or central hearing loss.[11] Although most studies have noticed the effects of hyperbilirubinemia on the brain stem, it seems that this disorder affects cochlea as well (at least the region involved in the processing of high frequencies). Some studies reported that the organ of Corti lesions especially at the outer hair cells and the cochlear nerve causes auditory impairment after hyperbilirubinemia.[12] Gupta et al[13] showed the presence of auditory neuropathy in about 5.5% of hearing impaired infants. Thirteen (19.2%) out of 68 neonates in an intensive care nursery with one or more adverse perinatal clinical factors were diagnosed to have hearing impairment by BERA testing. Among various risk factors, only 2 factors have been significantly correlated to hearing impairment in the affected neonates [viz; hyperbilirubinemia at level exceeding indication for exchange transfusion & birth weight (<1500gm).[13] Isman Jafar et al[14] found that increase in BERA latency in neonates with hyperbilirubinemia is more significant for the later waves (III and V) than for the earlier waves, and that the I-V interval increased significantly. These results suggest that there is also central auditory impairment after neonatal hyperbilirubinemia, in addition to peripheral auditory impairment. Study by Isaman Jafar[14] also shows the prolonged latencies in interpeak latencies I-III, I-V and also wave V. There was no peripheral nerve impairment (prolong wave I) in this study. The study by Isaman Jafar[14] shows that in moderate hyperbilirubinemia (10-20mg/dl), neurotoxicity is uncommon, and did not have strong correlation with BERA abnormality. This supports our finding of increased wave V latency and inter-peak latency I-V[14]. Other studies by Jiang[15] (>20 mg/dl), Sharma[16] and Agarwal[17], also Gupta [18] (>30 mg/dl), with higher bilirubin level showed strong relation between the bilirubin level and BERA abnormality. Dorothy et al[19] found the 100% sensitivity of BAEP as a screening test, with 86% specificity. With further experience & technological advances, use of BAEP for wide-spread clinical utilization in the hearing screening of high –risk newborns. Ze Dong Jiang et al[20] observed that there were no major differences in BAER variables between the neonates with different levels of TSB, except for a significant increase in wave V latency and I-V interval in the neonates with TSB greater than 20 mg/dL when compared with those with TSB at 11-15 mg/dL. This study substantiates our findings. By this study we can observe that infants exposed to neonatal jaundice are prone for some hearing abnormality which correlates with earlier school of thoughts as quoted below. As the bilirubin level increases the risk increases and those children need continuous follow up till the complete language development. Previous studies[21] have also concluded that many individual neonatal variables such as high serum bilirubin concentration, low Pao2 or cyanotic attacks were associated with loss of hearing ability. Bilirubin can deleteriously affect the auditory pathway anywhere along the brain stem, although the cochlear nucleus is the most usually involved.[22,23] A causative relationship between neonatal jaundice and irreversible brain stem damage has been established on the basis of clinic-pathologic correlations, audiometry and epidemiologic data. These findings may point to apparently specific functional lesion of hyperbilirubinemia, indicating severe neural damage with sparing of cochlear hair cells, has reinforced the contention that bilirubin toxicity involves the auditory pathways rather than the cochlea.[24] Bilirubin can deleteriously affect the auditory pathway anywhere along its course in the brainstem although the cochlear nucleus is usually most involved leading to hearing impairment.[23,25] Improved brain functions after phototherapy and /or exchange transfusion may be due to removal of bilirubin from brainstem. But persistence of abnormalities in some cases may be due to permanent damage caused by axonal degeneration and loss of myelin rather than hair cell loss.[26] So this hearing impairment has to be detected in the early stages and proper rehabilitative measures are taken at the earliest so that

further developmental milestones are not delayed. BERA as a screening procedure will give an idea of the degree of hearing impairment. BERA is the only tool which can confirm the normal sensitivity of hearing whenever required and is very useful in early detection of hearing loss; follow up of Neonatal hyperbilirubinemia patients with high bilirubin levels and the planning of rehabilitative procedures.

5. CONCLUSION

In our study there was an increase in wave V latency and I-V inter-peak latency in infants with higher bilirubin levels compared to the controls. Our study throws light on the effects of increased bilirubin levels on hearing ability. Since hyperbilirubinemia is a risk factor for hearing impairment, their hearing screening by BERA at the earliest will help in their earliest initiation of rehabilitation when the brain is sensitive to the development of speech and language. The hearing impairment has to be detected in early stages and proper rehabilitative measures are taken at the earliest so that further developmental milestones are not delayed. Type of treatment, either phototherapy or blood exchange, has no effect on the prevention of auditory neuropathy; therefore, appropriate measures (OAE and ABR) must be taken in the case of bilirubin higher than 20mg/dl. It should be mentioned that periodic assessment of the auditory system in hyperbilirubinemia is recommended because it is likely that the effects of hyperbilirubinemia on CNS can be reversible and hearing impairment may improve after a period. Acknowledgement: I would like to express my sincere thanks to all the staff of the Department of Physiology, JJM Medical College, Davangere, Dr. Guruprasad D. Neonatologist, Professor, Dept. of Neonatology, as well as staff and subjects of Bapuji Child Health Institute, Davangere and Dr.Shamshad Begum, Statician dept. of Psychiatry Bapuji Hospital, Davangere who have helped me in making this work a reality. Further studies are needed to know the bilirubin levels and their intensity of auditory impairment so that toxicity of bilirubin on hearing can be quantified. Studies have to be planned for a follow-up on hyperbilirubinemia infants to evaluate the bilirubin toxicity.

6. AUTHORS CONTRIBUTION STATEMENT

Dr. Bhagya V Conceptualized and designed the work. The data collection was done by Dr. Manjushree R. Data analysis and interpretation was done by Dr. Shamshad Begum.

7. CONFLICT OF INTEREST

Conflict of interest declared none.

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