Hearing Status in Neonatal Hyperbilirubinemia by Auditory Brain Stem Evoked Response and Transient Evoked Otoacoustic Emission

Mohammad Hossein Baradaranfar[1], Saeid Atighechi[1], Mohammad Hossein Dadgarnia[1], Rozita Jafari[1], Ghasem Karimi[1], Abolfazl Mollasadeghi[2], Zia Eslami[3], and Amin Baradarnfar[4]

[1] Department of Otolaryngology, Head and Neck Surgery, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

[2] Department of Audiology, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

[3] Department of Pediatrics, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

[4] Student of Medical School, Tehran University of Medical Sciences, Tehran, Iran

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Abstract- Hyperbilirubinemia at neonatal period is one of the major deteriorating factors of the auditory system. If left untreated, it may cause certain cerebral damage. This study aims to evaluate the impact of hyperbilirubinemia on the hearing of neonate. This study was conducted on 35 newborn babies with jaundice (bilirubin more than 20 mg/dL). Auditory brainstem response (ABR) and transient evoked otoacoustic emission (TEOAE) tests were performed, after treatment and one year after. ABR test results indicated that 26 children (74.3%) had normal hearing but 9 (25.7%) suffered from an impairment. As for TEOAE test, 30 children (85.7%) passed whereas the remaining (14.3%) seemed to be failures. The comparative results of the two tests pointed to autonomic neuropathy /autonomic dysreflexia symptoms in 5 babies. Due to the high incidence of Autonomic neuropathy/autonomic dysreflexia among hyperbilirubinemic babies, screening in this regard seems reasonable. Our result emphasizes the necessity of more experiments on the afflicted areas.

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Introduction

Autonomic neuropathy/autonomic dys-synchorny (AN/AD) is not a newly known disorder, but recently it has been possible to more accurately assess and understand it. Auditory neuropathy is defined as hearing impairment with normal outer hair cells and cochlea, but impaired neural conduction in auditory pathways (1, 2). This condition (or other conditions with similar pattern) accounts for 7% of permanent childhood hearing losses and a significant percent of adulthood hearing impairments (3). The most frequent infantile problems accompanying AN/AD include, anoxia and hyperbilirubinemia. Early incidence of one or both of these problems has been reported in more than 50% of cases.

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 (unbound to albumin) is increased this form of bilirubin can cross blood-brain barrier and precipitate in different parts of nervous system, such as basal ganglia, brainstem, cerebellum, and hypocampus. Although most infantile hyperbilirubinemia (60%) are physiologic and harmless (5), 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, which shows the sensitivity of both peripheral and central auditory systems to bilirubin.

In general, audiologic signs in AN/AD include: (1,2) 1. Weak speech discrimination score (SDS) and lack of accordance with average hearing threshold (PTA); 2. lack of acoustic reflex, absence of ABR recordings or abnormal results; 3. normal cochlear micriphonic (CM) and/or otoacoustic emissions (OAE). So we decided to evaluate the impact of hyperbilirubinemia on the auditory ability of neonatal by using auditory brain stem

Corresponding Author: Mohammad Hosein Baradaranfar
Department of Otolaryngology and Head and Neck Surgery, School of Medicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran
Tel: +98 351 8224000, Fax: +98 351 8224100, E-mail: baradaranf@ yahoo.com

response (ABR) and transient otoacoustic emissions (TEOAE) tests.

Materials and Methods

In this study, we evaluated hyperbilirubinemic infants (bilirubin>20mg/dl) who were admitted to neonatal intensive care units (ICUs) in all university hospitals of Yazd, Iran. All of the infants were referred to Shahid Rahnamoun hospital audiometry clinic for assessment of hearing difficulties after a complete course of treatment. Among 60 referred infants, after exact assessment of risk factors affecting hearing, prior hearing injury, and detailed history taking, 40 patients entered the study, but 5 other patients were excluded from the study afterwards. Exclusion criteria included: birth asphyxia, craniofacial anomalies, history of familial hearing loss, infections (TORCH), and G6PD (glucose 6-phosphate dehydrogenase) deficiency.

In order to find any disorder in the middle ear, after examination by otoscope, tympanometry was performed for all the cases (tympanometer, Cappela, Madsen, Denmark). After confirmation of lack of any disorder in the middle ear, TE-OAE (transient evoked OAE) was performed for all the cases (TE-OAE device: Cappela, Madsen, Denmark). Afterwards, all the infants underwent ABR (ABR device, AEP, model EP15, Denmark) by monoaural method during sleep. Stimulus was administered by insert headphones (ER3). bicanal electrode (inverting electrode on mastoid, and non-inverting electrode on forehead, and ground electrode on cheek) was used to record signal. Test parameters were as follows: time window 0-15 ms, average response 2000 times, rate of 11.2 stimulus/second, and stimulus intensity of 90 dBnHL. Absolute latencies of waves I, III, and V, and inter-wave latencies of I-III, III-V, and I-V waves were measured at 90 dBnHL. In order to identify the hearing threshold for wave V, stimulus intensity was lowered by 20dB intervals. The criterion for normal hearing was the presence of wave V in stimulus intensity of 20 dBnHL.

Tests were repeated 1 year later (from january 2009 till february 2010). A weight, age, and method of delivery matched control group was used to analyze data. Statistical Package for Social Sciences (SPSS; version 16.0) was used for data analysis. Descriptive statistics, chi square, Fisher exact and t tests were used for the analysis.

Results

Twenty female and 15 male infants were tested immediately after treatment. The control group consisted of 35 normal infants. According to their blood bilirubin level, patients were divided into 3 groups (table). Treatment method was phototherapy in 31 cases (94.3%) and exchange transfusion in 4 infants (5.7%): 4 transfusions for 1 infant (1.4%), 2 transfusions for one infant (1.4%), and 1 transfusion for 2 infants (2.9%).

OAE was performed for all of them immediately after treatment. In the first stage, 20 infants were passed. For other 15 infants, in the repeated OAE 10 other infants were passed (On the whole 30 infants or 85.7% were passed). Comparing control and case groups, we couldn't find a statistically significant difference (P value= .54). Twenty-six infants (74.3%) had normal ABR. Among other 9 with abnormal ABRs, 5 had no ABR waves at all and 4 had increased I-III and III-V intervals and latency in all waves. This difference was statistically significant (P value= .002). According to ABR, 26 (74.3%) had normal hearing, 4 (11.4%) mild to moderate hearing loss, and 5 (14.3%) suffered from severe to profound hearing loss. These results showed a significant difference in comparison with the control group. Blood bilirubin level in four infants with severe to profound hearing loss was more than 30 mg/dL, and in patients with mild to moderate hearing loss 3 had bilirubin level more than 30mg/dL, and one infant had bilirubin level between 20 and 25 mg/dL.

OAE could be recorded in 1 infant with mild to moderate hearing loss and 4 infants with severe to profound hearing loss. Overall, considering the results of ABR and OAE, 26 infants (76.5%) had normal tests and in 5 patients with abnormal results (14.3%) the site of pathology could be localized in retro-cochlear region, so they seemed to suffer from auditory neuropathy. Retesting these cases after 1 year showed that only one of the cases suspected to had neuropathy (with mild to moderate hearing loss) had normal ABR, and no change happened in other cases.

Table 1. Bilirubin level category

Patient Category	Bilirubin level	Frequency	Female/Male
1	20-25	20 (79.5%)	12/8
2	25-30	8 (11.4%)	3/5
3	>30	7 (10%)	5/2

Discussion

Hyperbilirubinemia is one of the most important problems during infantile period. In its severe form, it affects brain and causes kernicterus. This disease is caused due to precipitation of bilirubin in nervous tissue. Basal ganglia, various nuclei in the brain stem, cerebellum, and hypocampus are the most affected organs. Damage to these structures can cause cerebral palsy, mental retardation, and sensorineural or central hearing loss (6, 7). Prevalence of severe hyperbilirubinemia has increased in the past 2 decades. Studies have proposed causes for this increased incidence as decreased anxiety about birth time icterus, early discharge of the infants after birth (before 24-48 hours), inadequate follow-up of infants with hyperbilirubinemia, and incomplete medical staff knowledge about adverse effects of hyperbilirubinemia (4, 6, 8). In this study, we used OAE and ABR to assess auditory system in individuals with hyperbilirubinemia. Hearing threshold was considered as the presence of wave V in ABR with the minimum stimulus intensity. This cannot be interpreted as a real hearing threshold or behavioral threshold. In this study, TE-OAE was recorded in more than 85% of cases, consistent with Sheykholeslami and Kaga (5). 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). Results of this study confirm the inadequacy of TE-OAE alone for assessing auditory system. Although OAE was normal in 85.7% of the cases, ABR was abnormal in 25.7% of them. According to the criteria for identifying hearing loss in our study, 4 infants (11.4%) and 5 infants (14.3%) suffered from mild to moderate, and severe to profound hearing loss respectively. In 5 infants suffering from hearing loss, TE-OAE was normal, but ABR was abnormal. Among these 5 cases, 4 infants had severe to profound hearing loss and 3 of them were treated by exchange transfusion and the remaining one whose bilirubin level was 20-25mg/dL, was treated by phototherapy. These results define normal cochlear function in these 5 infants. This finding shows the presence of the auditory neuropathy in about 5.5% of hearing impaired infants. Therefore, mis-diagnosing infants suspected to auditory neuropathy and high level of false negative results, are the main shortcomings of TE-OAE. This may delay their access to therapeutic and rehabilitation facilities.

Although the main location of damage in hyperbilirubinemia and Kernicterus is the auditory nuclei in the brain stem, cochlear implant has been successful in development of oral skills (9). 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.

In the initial assessment, one patient suffering from mild to moderate hearing loss had normal hearing thresholds after a period. This issue has been also confirmed in other studies (10-13). Thus, hearing loss observed in these studies is not necessarily permanent and it may reverse after a while. The prevalence of hearing loss in hyperbilirubinemia patients is variable in different studies. Claros *et al*. in a study of 7 infants with hyperbilirubinemia, showed 2 cases of sensorineural hearing loss (14). Because of various factors affecting hearing loss in infants, detection of the precise effect of hyperbilirubinemia in hearing loss is difficult. In our study all the infants showing auditory neuropathy had hearing loss in ABR. We tried to exclude all other risk factors affecting hearing loss in the infants, but there may be some unknown confounding factors. This again emphasizes on necessity of more studies for complete assessment of hyperbilirubinemia effect on hearing loss (5). In conclusion, in spite of large developments in medicine in recent years, hyperbilirubinemia and its effects on sensory and motor systems is still an important problem. Because the effect of hyperbilirubinemia on hearing nuclei in the brainstem is one of the earliest effects of this biochemical disorder, it is necessary to perform physiologic tests that are sensitive enough to the target organ of hyperbilirubinemia in order to find its functional effects, severity, and possible appropriate treatment. Because of high incidence of AN/AD in infants with hyperbilirubinemia, it is recommended to perform at least ABR and OAE, especially in screening programs for the auditory system. 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 20% mg /dL.

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