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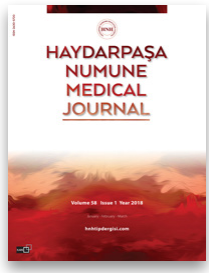

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ORIGINAL ARTICLE

The Effect of Bilirubin Levels on Results of Auditory Screening in Newborns

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Abstract

Introduction: To evaluate the effect of bilirubin levels on auditory screening results in newborns.

Methods: In total, 43 newborns (24 males and 19 females) who underwent the neonatal auditory screening in our hospital were included in the present study. All newborns were evaluated before they were discharged from the hospital. They were divided into two groups according to the results of the screening. Group A consisted of newborns that cleared the screening, whereas group B consisted of the remaining cases.

Results: There were 31 newborns (16 males, 15 females) in group A and 12 newborns (8 males, 4 females) in group B. In group A, mean total serum bilirubin level was 24.7±8.1 mg/dl, mean serum indirect bilirubin level was 23.3±8.0 mg/dl and mean serum direct bilirubin level was 1.1±1.6 mg/dl. In group B, these values were 28.1±6.6 mg/dL, 27.1±6.4 mg/dL, and 1.4±1.3 mg/dL, respectively. There were no statistically significant between-group differences between total serum bilirubin levels, indirect, and direct serum bilirubin levels (p-values: 0.279, 0.168, and 0.233, respectively). There was no significant difference between hematocrit, reticulocyte, leukocyte, and platelet values of the groups (all p-values >0.05).

Discussion and Conclusion: The results of the newborn auditory screening were not affected by serum bilirubin levels. However, the clinician should consider that the neonatal jaundice is a risk factor for hearing loss.

Keywords: Hearing screening; hearing loss; newborn; serum bilirubin level.

Neonatal jaundice is frequently seen in approximately 60% of term babies and approximately 80% of preterm babies in the first week of life [1,2]. The diagnosis, follow-up, and treatment stages of neonatal jaundice are important. It is thought that there is a relationship between the increase in serum bilirubin levels and the development of neurological complications [3,4]. Although many studies have been conducted on this subject, a clear relationship between the two has not fully emerged yet. In spite of recent advances in medicine, the effects of high bilirubin levels on the neurological system remain a serious problem.

Central hearing pathways are one of the most frequently affected pathways from bilirubin toxicity in the central nervous system [5]. The normal hearing function is ensured by the compatibility of activity between the nervous system cells. Hearing deficiencies occur as a result of impaired neuronal compliance and disturbed hearing pathways.

The type of bilirubin which is effective in the development

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of bilirubin toxicity is free indirect bilirubin [3]. Free indirect bilirubin leads to disruption of this neuronal compliance by crossing the blood-brain barrier. In neonatal jaundice, sensorineural hearing loss may develop as a result of the toxic effects of indirect bilirubin on the central nervous system.

Auditory screening tests are performed on every baby born in hospitals before being discharged and are regularly followed-up in babies who are at risk of hearing loss. The National Newborn Hearing Screening Campaign that was initiated under the leadership of the Ministry of Health and some universities and has now become widespread throughout the country [6].

The group which is at risk of hearing loss consists of infants with intrauterine infections, head trauma, low birth weight, neonatal jaundice, metabolic syndrome, and babies hospitalized in intensive care units [3,4].

Numerous medical guidelines have been published to protect neonates from neurological complications of hyperbilirubinemia [7–9]. It has been suggested that newborns should be regularly and effectively followed-up for the early detection, treatment, and prevention of potential complications [8,9]. About 40% of newborns with hyperbilirubinemia are at risk of hearing loss [10].

The aim of this study was to investigate the relationship between total serum bilirubin levels and screening test results of infants undergoing phototherapy with the indication of neonatal jaundice in the neonatal intensive care units of our hospital.

Materials and Methods

This retrospective clinical study was performed between January 2009 and January 2012 in the Neonatal Intensive Care Unit and Otorhinolaryngology Surgery Clinic of our hospital. The study was conducted in accordance with the guidelines of the Good Clinical Practices Guide and the 2008 Helsinki Declaration. The study was approved by the Clinical Research Ethics Committee of the same hospital (Ethics Committee no: 2017-131).

The study included 43 newborns (24 males, 19 females) who were either born in our hospital or were referred to our hospital from the neonatal hearing screening department, and were hospitalized in the neonatal intensive care unit with serum bilirubin levels higher than 15 mg/dl. Hearing screening tests were performed 24 hours after birth and after phototherapy was completed. The infants who were intubated after birth, newborns with intrauterine infection, sepsis, meningitis or encephalitis, conjugated hyperbilirubinemia, middle and external ear pathology, and syndromic and congenital malformations were excluded from the study.

Type of delivery, birth weights, and head circumferences of all newborns were recorded. All patients underwent phototherapy and complete blood exchange. Phototherapy time was determined according to nomograms prepared as per birth weights and birth times of the newborns. The mean duration of phototherapy was 12.48±8.02 days (range: 4–22 days).

Neonatal hearing screening tests were performed by audiometry technicians in an isolated room dedicated as the audiology laboratory in a building used only for auditory screening tests. While recording the measurements, it was preferred that the baby be asleep or immobile. The most suitable pediatric probe tips were used, according to the size of the external ear canal.

Otometrics Accuscreen® otoacoustic emission device (GN Otometrics A/S, Denmark) was used to apply the Transient Evoked Otoacoustic Emissions (TEOAE) method in the auditory screening tests. A satisfactory response was considered when a positive emission was obtained during otoacoustic emission measurements in at least three frequency bands out of the four bands that were tested (1 kHz, 1.4 kHz, 2 kHz, 2.8 kHz, 4 kHz). Newborn babies were divided into two groups according to the screening test results. Group A consisted of newborns that passed the screening tests while group B consisted of cases that failed the test.

Blood samples from the heels of the babies were withdrawn within the first 24 hours after birth and their hematocrit, C-reactive protein (CRP), leukocyte count, platelet count, and direct, indirect and total bilirubin values were compared.

Statistical Analyses

For statistical analyses, the NCSS 2007 program (Number Cruncher Statistical System, Kaysville, Utah, U.S.A.) was used. While evaluating the study data, mean, standard deviation, median, frequency, ratio, minimum, and maximum were used in descriptive statistical methods. The distribution of variables was measured by the Kolmogorov-Smirnov test. Mann-Whitney U test was used to analyze the quantitatively independent data.

Results

Demographic characteristics of the cases included in the study are given in Table 1. The mean age of the patients included in the study was 3.8 ± 3.2 days (range: 2–14 days). Group A consisted of 31 newborns (16 male, 15 female) and Group B consisted of 12 newborns (8 male, 4 female).

The mean total serum bilirubin, indirect serum bilirubin, and direct serum bilirubin levels in Group A patients were 24.7±8.1 mg/dl, 23.3±8.0 mg/dl, and 1.1±1.6 mg/dl, respectively. In Group B, the corresponding values were 28.1±6.6 mg/dl, 27.1±6.4 mg/dl, and 1.4±1.3 mg/dl, respectively. There was no statistically significant difference between serum total serum bilirubin, indirect, and direct bilirubin levels between Groups A and B (p-values: 0.279, 0.168, and 0.233, respectively).

There was no significant difference in hematocrit, reticulocyte, leukocyte, and platelet values of the groups (for all: p>0.05) (Table 2). Eleven cases in Group A and two cases in Group B had total serum bilirubin levels less than 20 mg/dl. A statistically significant difference was not found between hearing screening test results according to total serum bilirubin levels of 20 mg/dl in both the groups (p>0.05) (Table 3).

Discussion

With an increase in the serum bilirubin levels, indirect bilirubin can pass through the blood-brain barrier and cause acute encephalopathy. While the emergence of neurological sequelae due to bilirubin toxicity does not follow an exact sequence, hearing problems tend to arise due to the central hearing pathways getting affected [3]. In the current study, we have studied the possibility of preventing central toxic effects of bilirubin by facilitating early treatment and rehabilitation.

Several studies have reported on the component of the hearing mechanism that is highly exposed to the harmful effects of bilirubin toxicity. It is thought that these components are the auditory nuclei in the brain and the inferior colliculus [11]. Shaia et al. [12] reported in their experimental study on rats that spiral ganglion neurons and myelinated hearing nerve fibers were also affected by bilirubin toxicity. The toxic effects of bilirubin are thought to manifest at the central level and do not cause any cochlear pathological findings. In their autopsy study, Haustein et al. [13] reported that cochlear functions were not affected in cases of bilirubin toxicity.

Abdollahi et al. [14] reported that there was no significant difference between normal neonates and neonates with hyperbilirubinemia in TEOAE. While detecting bilirubin toxicity, it is necessary to use objective tests to evaluate central hearing pathways. Hung suggested conducting auditory brainstem responses (ABR) to assess the auditory nerve and central hearing center in neonates with hyperbilirubinemia [15]. In this study, a hearing screening test was performed with TEOAE. While cochlear pathologies can be evaluated with TEOAE, central hearing pathologies cannot be detected. Therefore, the central effects of bilirubin toxicity could not be evaluated in our research.

Table 1. Demographic characteristics of the cases

	Min-Max	Aver±SD/n, (%)
Type of delivery		
Natural		27, (62.8)
Cesarian section		16, (37.2)
Gender		
Female		19, (55.8)
Male		24, (44.2)
Birth weights (gr)	2340-4350	3184±395
Birth length (cm)	44-54	49.9±2.2
Head circumferences at birth (cm)	31-39	34.6±2.0
Pregnancy week	35-41	39.3±1.2
Total Serum Bilirubin (mg/dl)	15-33	25.7±7.8
Indirect Serum Bilirubin (mg/dl)	16-31	24.4±7.7
Direct Serum Bilirübin (mg/dl)	1-9	1.2±1.5
Hematocrit (%)	26-59	42.8±8.9
Reticulocyte counts	0-25	6.5±6.2
CRP (mg/dl)	0-6	0.6±1.1
WBC counts/ mm^3 ($x10^3$)	6-106	17.5±15.5
Platelet counts/ mm^3 ($x10^3$)	38-681	291.6±111.3

Table 2. Intergroup comparisons of blood parameters

	Group A (n=31) Mean±SD	Group B (n=12) Mean±SD	p
Total Serum Bilirubin	24.7±8.1	28.1±6.6	0.279[m]
Indirect Serum Bilirubin	23.3±8.0	27.1±6.4	0.168[m]
Direct Serum Bilirubin	1.1±1.6	1.4±1.3	0.233[m]
Hematocrit (%)	40.6±4.8	43.2±6.9	0.412[m]
Reticulocyte counts	5.8±4.3	6.7±8.1	0.326[m]
CRP (mg/dl)	0.2±1.5	0.7±1.4	0.174[m]
WBC counts/ mm^3 ($\times10^3$)	16.2±14.9	17.8±15.2	0.942[m]
Platelet counts/ mm^3 ($\times10^3$)	286.2±108.1	292.1±112.4	0.262m

[m]Mann-Whitney U test.

Table 3. Intergroup comparisons of auditory screening test results with reference to total serum bilirubin levels

Total serum bilirubin levels	Group A (n=31)	Group B (n=12)	*p
>20 mg/dl	11 (35.4)	2 (16.7)	0.422
<20 gm/dl	20 (64.6)	10 (83.3)	0.086

*Mann-Whitney Test.

The relationship between serum bilirubin level and hearing loss has been investigated in previous studies. No clear conclusions were found on the level of bilirubin levels in neonates who were at high risk for hearing loss. Sheykholeslami and Kaga reported that even a moderate increase in bilirubin levels could cause hearing loss [11]. In a recent meta-analysis, Akinpelu et al. [3] reported that keeping bilirubin levels below 20 mg/dl in term babies is important for the prevention of hearing abnormalities. However, ABR anomalies can be detected in newborns whose serum bilirubin level is between 11 and 25 mg/dl [16,17].

However, although high bilirubin levels induce ABR anomalies, these high levels do not always cause hearing loss. ABR anomalies have been reported in 10%–44.8% of neonates with bilirubin levels below 20 mg/dl (18–20). ABR anomalies have been reported in 35.1% of newborns with bilirubin levels above 20 mg/dl [3]. While the rates of ABR abnormalities were higher in patients with bilirubin levels above 20 mg/dl, ethnic origins are thought to play a role in different studies. In this study, among 30 patients with bilirubin levels greater than 20 mg/dl, 20 newborns (66.7%) passed hearing screening tests, while 10 newborns (33.3%) failed.

In previous studies, early discharge, inadequate information on the effects of hyperbilirubinemia and inability to perform hearing screenings on a regular basis have been reported to lead to the emergence of permanent effects of hyperbilirubinemia [3,18,20]. Berlin et al.[21] reported that 74 (28.4%) of 260 children with auditory neuropathy spectrum disorder had a history of hyperbilirubinemia.

Different results have been reported on hearing loss due to bilirubin toxicity. Kuriyama et al.[22] reported that hearing loss due to bilirubin was temporary and could be improved with reduced serum bilirubin levels. Ye et al.[23] reported that auditory neuropathy improved with decreasing bilirubin level. Abdollahi et al.[14] reported that the auditory anomaly is transient and that this anomaly can be improved with appropriate treatment. In this study, a hearing screening was performed with TEOAE used in newborn screening in our country. All patients underwent auditory screening tests before phototherapy and the patients were divided into two groups. No significant difference was observed in terms of total serum bilirubin levels, indirect levels, and direct bilirubin levels between the patients who passed and failed the screening tests. These results indicate that the toxicity of bilirubin is not at the cochlear level. After phototherapy, all patients were screened again and all patients passed screening tests. These findings suggest that the toxicity of bilirubin is transient and that auditory abnormalities show improvement in patients receiving appropriate treatment.

Our study had many limitations. Since the number of patients included in this study was relatively low, ABR was not used as a screening test. Besides the absence of a control group, the retrospective design of the study did not allow us to check whether hearing loss developed or not during their follow-up. There is a need for further studies with longer follow-up results where the auditory nerve and central hearing center will be evaluated using ABR.

Conclusion

In this study, the effect of bilirubin level on the results of neonatal hearing screening was investigated. All patients were screened at the end of phototherapy. We concluded that the bilirubin level did not have any effect on screening results. However, the clinician should consider that neonatal jaundice is a risk factor for hearing loss. Further studies should be performed with a greater number of patients in order to achieve a more accurate consensus.

Ethics Committee Approval: The study was approved by the Clinical Research Ethics Committee of the same hospital (Ethics Committee no: 2017-131).

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