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Comparison of the Efficacy of Auditory Steady-State Response (ASSR) and Otoacoustic Emission (OAE) in Neonatal Hearing Screening

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ABSTRACT

To investigate the correlation among auditory steady-state response (ASSR) and transient evoked otoacoustic emission (TEOAE) and screening brainstem auditory evoked response (s-BAER) tests in children with sensorineural hearing loss (SNHL).

TEOAE, multiple-ASSR, and click s-BAER recordings and analyses of 30 healthy newborns and 74 newborns with high-risk of SNHL were performed prospectively. The three techniques were compared between healthy and high-risk SNHL newborns. In addition, average test durations were calculated in minutes.

Hyperbilirubinemia requiring transfusion was the most common risk factor in the high-risk SNHL group. In the ASSR test, the rate of failure was higher at low frequencies and was dramatically lower at high frequencies. In both ASSR and TEOAE, the sensitivity and accuracy rates increased at high frequencies. Average test duration (including preparations) was 30.2±6.45 min for multiple-ASSR, 1.26±0.81 min for TEOAE, and 1.86±0.87 min for s-BAER.

Multiple-ASSR was found to be more sensitive in predicting behavioral hearing status compared to TEOAE. Based on our findings, we consider that multiple-ASSR is an objective test that can be used safely in predicting rapid frequency-specific behavioral hearing of bilateral ears simultaneously without requiring practitioner's interpretation, particularly in high-risk neonates. However, further evidence and studies are needed to ensure that the newborn's hearing prediction alone is sufficient.

Keywords: Newborn, auditory steady state responses, otoacoustic emission

Introduction

Incidence of neonatal hearing loss (HL) as a major birth defect ranges from 1/1000 to 6/1000 (1). It is highly difficult to assess the degree of HL in infants and thus there is little information in the literature regarding the prevalence of mild and moderate HL in this population (2). In children, diagnosing HL in the early stage and determining the ideal treatment approach are highly essential for supporting their speech and language development as well as their social, psychological, and educational development. Early diagnosis and treatment of HL is possible with neonatal hearing screening programs and auditory health programs (3). Most commonly used acoustic-immittance measurements in the diagnosis of HL include otoacoustic emission (OAE), brainstem auditory evoked response (BAER), and auditory steady-state response (ASSR). Studies have shown that administering speech and hearing therapies following appropriate audio amplification within the first six months of life maximizes the speech and hearing development potential of each child at the level of hearing loss (4,5).

The World Health Organization (WHO) has consistently placed this treatable health problem on the agenda and made recommendations for its early diagnosis. In 2010, WHO published an action plan with the aim of supporting Universal Newborn Hearing Screening (UNHS) (6). Through this plan, WHO suggested that *"all programs aimed at early diagnosis of hearing loss should be associated with the existing health, social assistance and education system..."*. Similarly, in 2007, the American Academy of Pediatrics Joint Committee on Infant Hearing (AAP/JCIH) recommended performing frequency-specific BAER in children younger than 6 months. However, the time-taking nature of this practice and the differentiation in interpretation

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based on the experience and knowledge of the practitioner have led to the search for different methods. With the advent of click screening-BAER (s-BAER), the event was automatically applied and the most easily detected V. wave was targeted and the answers were interpreted with computer programs and the results of "passed" and "failed" were aimed (7). However, since click s-BAER is not frequency-specific and stimulates the entire cochlea, the structure and degree of HL cannot be evaluated and studies have shown that there is a high rate of false-positives in the results obtained with click s-BAER (8,9).

In 2001, the auditory steady-state response (ASSR) technique was introduced, which is a novel electrophysiological test and enables the hearing to predict frequency-specific behavioral thresholds. Despite being in the developmental stage, this method is utilized for achieving the most accurate behavioral thresholds in awake and sleep states by using amplitude-modulated pure tones. The ASSR responses can be obtained by simultaneous delivery of a stimulus to both ears through the multiple-ASSR technique and the determination of the neural activity generated depending on each of the specific modulation frequencies (10). In this way, eight different frequencies, with four different frequencies in each ear, can be tested simultaneously, resulting in shorter test time. The ASSR test also strengthens the prediction of frequency-specific behavioral thresholds by performing functional masking to neighboring frequencies with simultaneous multiple stimuli (10,11). On the other hand, advanced and very advanced HL that cannot be detected in the auditory brainstem response (ABR) test can be detected with the ASSR test (3,12).

Reliable detection of HL in newborns with a high risk of HL is more difficult than in healthy newborns due to the presence of additional conditions (prematurity, hyperbilirubinemia) (8). In the evaluation of hearing in newborns, immittance values, OAEs, click and tone-burst BAER, and ASSR provide objective information about hearing although they provide limited information about the level, shape, and frequency distribution of HL. This scarcity of information is compensated by new studies and technological discoveries such as multiple-ASSR. Aural acoustic-immittance measurements are performed to exclude the tympanic membrane and middle ear pathologies in all newborns detected with hearing problems in ear examination. Examination of the acoustic nerve reflex arch performed with the same test device may provide partial information about hearing (13).

Transient evoked otoacoustic emissions (TEOAEs) are measured after the presentation of a short stimulus. TEOAEs employ the click stimulus with a broad spectrum or the tone-burst stimulus with a narrow frequency. TEOAE is one of the most widely used technique in clinical studies related to hearing. This test can be easily performed by following the instructions of the computer software. Major advantages of the test include non-invasiveness, non-requirement of comments or active participation of the patient, and rapid results (14). In addition, the technique has become as a first-line neonatal screening test due to its sensitivity in peripheral sensorineural HL (SNHL), high specificity in outer hair cell dysfunction, ease of application, low cost, and non-requirement of consumables (14-16).

The aim of this study was to investigate the correlations among the three tests used in screening children at risk of SNHL (ASSR, TEOAE, and s-BAER) and to compare their test durations.

Materials and Methods

Ethics Approval and Study Groups: This study was conducted in Van Yuzuncu Yil University Medical School Otorhinolaryngology Department. This study was reviewed and approved by Turkey Pharmaceuticals and Medical Devices Agency (Turkish Ministry of Health) and Yuzuncu Yil University Noninterventional Clinical Research Ethics Committee (Approval No: 04; Date: January 30, 2014). An informed consent was obtained from each parent/guardian. The study protocol was conducted in accordance with the principles of the Declaration of Helsinki and Guidelines for Good Clinical Practices.

Subjects were divided as (i) healthy newborns (healthy group) and (ii) newborns at high risk of SNHL (high-risk SNHL group). Subjects that fulfilled the criteria modified by the Joint Committee on Infant Hearing (JCIH) in 2007 were assigned to the high-risk SNHL group: (i) newborns with hyperbilirubinemia requiring transfusion, (ii) birth weight less than 1500 g, (iii) craniofacial anomalies, (iv) chromosomal abnormalities, (v) congenital infection (i.e. meningitis and sepsis), (vi) use of ototoxic drugs, (vii) mechanical ventilation lasting more than five days, (viii) postnatal asphyxia, (ix) cerebral intraventricular hemorrhage, and (x) family history of hearing loss (4).

Children whose parent/guardian did not provide a written consent, those that did not meet the SNHL criteria, had an underdeveloped external ear canal (since the tests were performed with by inserting earphones in the external ear canal), and those with tympanic membrane and middle ear disorders were excluded from the study. Accordingly, hearing screening was performed on 60 ears in 30 healthy newborns (16 boys and 14 girls) and on 148 ears in 74 newborns with SNHL (39 boys and 35 girls).

Study Protocol: An otoscopic examination of the external auditory canal, tympanic membrane, and middle ear was performed in each subject. Subsequently, acoustic-immittance measurements were performed using a calibrated tympanometer (Interacoustics AT235 Impedance Audiometer, Denmark). Subjects with type A curve were taken into a soundproof Faraday cage isolated from external magnetic fields by copper plating, where TEOAE, multiple-ASSR, and s-BAER tests were performed respectively. ASSR test results were confirmed by the ABR results. The tests were repeated for the samples that were found incompatible. Subjects that were found to be incompatible at the second test were excluded from the study. All the results obtained at 500, 1000, 2000 and 4000 Hz and the test durations were recorded. Test duration was measured using the microcomputer clock method.

TEOAE Protocol: Both the healthy and SNHL newborns were taken to Faraday cage. Healthy newborns were carried in their mother's lap and the SNHL newborns were in their mothers' laps or were anesthetized in the incubator. Measurements were recorded using a Echoport ILO 292 device (Otodynamics DP, Hatfield, UK) by means of a time domain averaging technique with click stimulus at alternating polarity of 80 to 86 dB SPL and at 1000 to 4000 Hz frequencies (17). The emission response was considered "passed" if 1) the repeatability of the emissions at the defined frequencies was ≥50%, 2) the number of stimuli reached 1000, and 3) the signal/noise (S/N) ratio of emissions in a minimum of three out of four frequencies was +3 dB SPL or above. In the subjects that could not fulfil these three criteria, the emission response was considered "failed" (17).

Multiple-ASSR Protocol: Preparation of the subject:

Following the TOAE test, hearing thresholds of the subjects were determined while they were in their caregivers' laps (as in natural sleep) or on a heated soft stretcher (sedated with chloral hydrate in the incubator) using a multiple-ASSR test (Smart EP-ASSR System, USA). Prior to the test, the skin on the forehead, right-left mastoid bone, and zygomatic bone were cleansed with conductive gel. Electroencephalography (EEG) disc electrodes made of silver chloride were placed on the right mastoid (A2), left mastoid (A1), forehead (f2), and zygomatic bone (fp2). For each simultaneous multiple stimuli, ER3A insert-earphones were inserted in bilateral ear canals. The recording was performed on the stimulated ear. Maximum stimulation level was 120 dB HL and the volume was increased repeatedly by 10 dB at a time. The inter-electrode impedance at 260 Hz was less than 6 kOhms.

Stimulation Protocol: Multiple stimulations to each ear consisted of four simultaneous tones at four carrier frequencies (500, 1000, 2000 and 4000 Hz). Modulation frequencies were applied to the left ear at 77, 85, 93, and 105 Hz and to the right ear at 79, 87, 95, and 103 Hz, respectively.

Recording Protocol: The ASSR recordings were performed using the Rotman MultiMASTER research system. Calibration of the stimulation was performed separately for each frequency. EEG responses were recorded using four silver-chloride disc electrodes. Interelectrode impedances were maintained below 6 kOhms. EEG was amplified 50000 times and a band-gap filter of 30-250 Hz was used at 80 Hz. The analog-to-digital conversion rate was set to 1250 Hz.

Analysis of Responses: All the ASSR responses were analyzed using the fast Fourier analysis (FFT) algorithm and were converted into frequency-containing information and analyzed. In the analysis of ASSR responses, the F value was calculated using the Rotman MultiMASTER research system. If the statistical significance reached a p value of <0.05, the ASSR response was considered "positive (passed)"; otherwise, it was considered "negative (failed)" (18).

S-BAER Protocol: All s-BAER measurements were performed at 40 dB nHL with 93 Hz click stimulus utilizing the intermediate module of the Smart EP-ASSR system. Since all the subjects underwent automatic ABR measurements following ASSR measurements, the preparation phase was not repeated and the recordings were performed automatically. Accordingly, measurement results were considered "passed" or "failed".

Statistical Analysis: Data were analyzed using SPSS 24.0 for Windows (Armonk, NY: IBM Corp.). Quantitative variables were expressed as

mean ± standard deviation (SD) and categorical variables were expressed as frequencies (n) and percentages (%). Categorical variables were compared using Chi-square test. Diagnostic test statistics were calculated to determine positive (passed) and negative (failed) status, and to determine the performance of the ASSR method. A p value of <0.05 was considered significant.

Results

The study included 104 subjects (30 healthy and 74 SNHL infants) with a mean age of 12.01±9.58 (range, 2-47) days. Multiple-ASSR could not be performed in one healthy newborn and the click s-BAER test could not be performed in three newborns in the high-risk SNHL group.

Based on the JCIH classification, the most common risk factor in our patients was hyperbilirubinemia requiring transfusion (n=29, 39.18%), followed by birth weight less than 1500 g (n=19, 25.67%), craniofacial anomalies (n=12, 16.21%), chromosomal anomalies (n=6, 8.10%), congenital infection (n=6, 8.10%), and use of ototoxic drugs (n=2, 2.70%). However, no subject was detected with postnatal asphyxia, intraventricular hemorrhage, family history of HL, and requirement of mechanical ventilation lasting more than 5 days.

Table 1 presents the test results and ear distributions of the subjects in the high-risk SNHL group. Accordingly, 46 (31.08%) newborns failed in the TEOAE test, among whom subjects with hyperbilirubinemia (16/46) had the highest failure rate, followed by subjects with birth weight less than 1500 g (15/46), craniofacial abnormalities (6/46), chromosomal abnormalities (4/46), congenital infection (4/46), and use of ototoxic drugs (1/46). On the other hand, 9 (6.08%) subjects failed in the multiple-ASSR test, among whom subjects with craniofacial anomalies (5/9) had the highest failure rate, followed by subjects with hyperbilirubinemia (2/9), chromosomal abnormalities (1/9), and use of ototoxic drugs (1/9). In the s-BAER test, 24 subjects failed the test, among whom subjects with a birth weight less than 1500 g (12/24) had the highest rate, followed by subjects with hyperbilirubinemia (5/24), craniofacial anomalies (4/24), and chromosome anomalies (3/24).

Table 2 presents a comparison of TEOAE and s-BAER test results of both groups. In the TEOAE test, a total of 23 (23.1%) right ears and 27 (26%) left ears failed the test. Moreover, four (6.66%) ears in the healthy group and 46 (31.08%) ears in the high-risk SNHL group failed test. In the s-BAER test, two (6.6%) ears failed the test in the healthy group as opposed to 25 (35.2%) ears in the high-risk SNHL group.

Table 3 presents the frequency-specific multiple-ASSR results of newborns both groups. Accordingly, the number of subjects failing in the test at low frequencies was higher than that of subjects failing at high frequencies. A total of 44 (42.3%) right ears and 40 (38.5%) left ears failed the test at 500 Hz, while 4 (3.8%) right ears and 5 (4.8%) left ears failed the test at 4000 Hz. In the healthy group; 8 subjects failed the test at 500 Hz and only one subject failed the test at 1000 Hz, while no subjects failed the test at 2000 and 4000 Hz. In the high-risk SNHL group, 75 (50.68%) out of 148 ears failed in the test at 500 Hz and the rate of failure decreased dramatically at higher frequencies, whereby 39 (26.4%), 13 (8.8%), and 8 (5.47%) subjects failed the test at 1000, 2000 and 4000 Hz, respectively.

Table 4 presents a comparison of the high-risk SNHL group and all subjects with regard to TEOAE and ASSR results. In all subjects, the sensitivity of the test increased with higher frequencies, whereby the sensitivity at 500 Hz was 70.1% and was 100% at 4000 Hz. Similarly, the accuracy rate also increased at higher frequencies and reached the highest rate of 79.81% at 2000 Hz. However, the specificity rate decreased with increasing frequency. In the high-risk SNHL group, similar trends were observed in the sensitivity, specificity, accuracy rates.

Table 5 presents a comparison of the high-risk SNHL group and all subjects with regard to ASSR and s-BAER results. In both the high-risk SNHL group and all subjects, the highest sensitivity rates were observed at 2000 and 4000 Hz and the specificity rates decreased as the frequency increased. In the high-risk SNHL group, 12 (15.49%) right ears and 13 (19.71%) left ears failed the test and the best results were obtained at 2000 and 4000 Hz. At 4000 Hz, 3 (4.1%) right ears and 5 (6.8%) left ears failed the test. In the comparison of ASSR and s-BAER measurements in the high-risk SNHL group, the sensitivity was the highest at 2000 and 4000 Hz and the lowest at 500 Hz. In both the high-risk SNHL group and all subjects, the specificity rates decreased as the frequency increased.

Table 6 presents the average test durations for TEOAE, multiple-ASSR, and click s-BAER.

Table 1: Test Results in the High-Risk SNHL Group

Concomitant Diseases	Number of Newborn Ears (n) x2	Ear	Hearing Loss Detected Ears		
			TEOAE	ASSR 4000 Hz	s-BAER
Hyperbilirubinemia	58	Right	6	1	2
		Left	10	1	3
Birth weight less than 1500 g	38	Right	8	0	6
		Left	7	0	6
Cranio-facial anomalies	24	Right	3	2	2
		Left	3	3	2
Chromosomal anomalies	12	Right	1	0	1
		Left	3	1	2
Congenital infection	12	Right	2	0	0
		Left	2	0	0
Use of ototoxic drug	4	Right	0	0	0
		Left	1	1	0
Total Ear (%)	148 (100%)		46 (31.08%)	9 (6.08%)	24 (16.21%)

ASSR: Auditory steady-state response, s-BAER: Screening brainstem auditory evoked response, TEOAE: Transient evoked otoacoustic emissions

Table 2: TEOAE and s-BAER Results

Test		Ear	Passed n (%)	Failed n (%)	Total (n)
Newborn TEOAE	Healthy	Right	27 (90)	3 (10)	30
		Left	29 (96.7)	1 (3.3)	30
	High-risk	Right	54 (72.6)	20 (27.4)	74
		Left	48 (64.4)	26 (35.6)	74
	Total	Right	81 (76.9)	23 (23.1)	104
		Left	77 (74)	27 (26)	104
Newborn s-BAER	Healthy	Right	29 (96.7)	1 (3.3)	30
		Left	29 (96.7)	1 (3.3)	30
	High-risk	Right	59 (83.09)	12 (15.49)	71
		Left	58 (80.28)	13 (19.71)	71
	Total	Right	88 (87.12)	13 (12.87)	101
		Left	87 (86.13)	14 (13.86)	101

s-BAER: Screening brainstem auditory evoked response, TEOAE: Transient evoked otoacoustic emissions

Accordingly, average test duration (including preparations) was 30.2±6.45 min for multiple-ASSR, 1.26±0.81 min for TEOAE, and 1.86±0.87 min for s-BAER.

Discussion

The accuracy of behavioral thresholds achieved by ASSR and other tests has been compared in numerous studies in the literature (8,13,19-21). In our study, we compared ASSR with a test method proposed by the Turkish Ministry of Health for newborn hearing screening named TEOAE. To that end, healthy newborns and newborns with a high SNHL risk were compared with regard to their TEOAE, multiple-ASSR, and click s-BAER results.

Universal Newborn Hearing Screening (UNHS) recommends hearing screening within the first four weeks after birth. The UNHS programs target the infants that have not been discharged from the hospital after delivery or those aged less than 15 days and these programs aim to detect risky infants in the earliest stage (22). In our study,

Table 3: ASSR Results

ASSR TEST RESULTS	Frequency (Hz)	Ear	Passed n (%)	Failed n (%)
Healthy Group	500	Right	25 (83.3)	5 (16.7)
		Left	27 (90.0)	3 (10.0)
	1000	Right	29 (96.7)	1 (3.3)
		Left	30 (100)	0
	2000	Right	30 (100)	0
		Left	30 (100)	0
	4000	Right	30 (100)	0
		Left	30 (100)	0
High-risk Group	500	Right	36 (47.9)	38 (52.0)
		Left	37 (50.7)	37 (49.3)
	1000	Right	56 (75.3)	18 (24.7)
		Left	53 (71.2)	21 (28.8)
	2000	Right	69 (93.2)	5 (6.8)
		Left	66 (89.0)	8 (11.0)
	4000	Right	71 (95.9)	3 (4.1)
		Left	69 (93.2)	5 (6.8)
All Newborns	500	Right	60 (57.7)	44 (42.3)
		Left	64 (61.5)	40 (38.5)
	1000	Right	84 (80.8)	20 (19.2)
		Left	82 (78.8)	22 (21.2)
	2000	Right	99 (95.2)	5 (4.8)
		Left	96 (92.3)	8 (7.7)
	4000	Right	100 (96.2)	4 (3.8)
		Left	99 (95.2)	5 (4.8)

Table 4: Comparison Between ASSR and TEOAE in the High-risk Group and All Newborns

	Frequency (Hz)	Ear	Sensitivity (%)	Specificity (%)	Accuracy (%)	*p
High-risk Group	500	Right	56.6	75.0	42.47	0.016
		Left	59.6	65.4	61.64	0.041
	1000	Right	81.1	40.0	69.86	0.062
		Left	83.0	50.0	71.23	0.003
	2000	Right	98.1	20.0	76.71	0.006
		Left	97.9	26.9	72.60	0.001
	4000	Right	98.1	10.0	79.98	0.119
		Left	100.0	19.2	71.23	0.002
All Newborns	500	Right	66.3	70.8	67.30	0.001
		Left	70.1	63.0	67.8	0.002
	1000	Right	87.5	41.7	76.92	0.001
		Left	88.3	48.1	77.89	0.001
	2000	Right	98.8	16.7	79.81	0.002
		Left	98.7	25.9	79.81	0.001
	4000	Right	98.8	12.5	78.85	0.012
		Left	100	18.5	78.85	0.001

**Chi-square test*

Table 5: Comparison Between ASSR and s-BAER in the High-Risk Group and All Newborns

	Frequency (Hz)	Ear	Sensitivity (%)	Specificity (%)	Accuracy (%)	*p
High-risk Group	500	Right	59.3	100.0	63.00	0.000
		Left	61.4	92.3	80.00	0.002
	1000	Right	50.0	96.4	84.93	0.000
		Left	84.2	84.6	83.56	0.000
	2000	Right	100.0	45.5	91.78	0.001
		Left	94.7	38.5	84.93	0.002
	4000	Right	100.0	27.3	89.04	0.001
		Left	96.5	23.1	83.56	0.037
All Newborns	500	Right	67	100	71	0.001
		Left	70.1	92.3	73	0.001
	1000	Right	90.9	83.3	90	0.001
		Left	88.5	84.6	88	0.001
	2000	Right	100	41.7	93	0.001
		Left	96.6	38.5	89	0.001
	4000	Right	100	33.3	92	0.001
		Left	97.7	23.1	88	0.001

**Chi-square test*

Table 6: Average test durations for both ears in all tests

Tests	N	Mean	SD	Minimum	Maximum
TEOAE	104	1.26	0.81	0.33	3.00
s-BAER	104	1.86	0.87	1	4
ASSR	104	30.2	6.458	15	60

ASSR: Auditory steady-state response, s-BAER: Screening brainstem auditory evoked response, TEOAE: Transient evoked otoacoustic emissions

the hearing test in the healthy group was performed prior to hospital discharge and the test in the high-risk SNHL group was performed as soon as the patient presented a good general health condition.

In our study, 6.66% of healthy newborns (60 ears) did not pass the TEOAE test, while all the healthy ears passed the ASSR test at 2000 and 4000 Hz. On the other hand, two newborns did not pass the s-BAER test bilaterally, which could be interpreted as a false positive result in the s-BAER test (9).

In our study, hyperbilirubinemia requiring transfusion was the most common risk factor (39.18%), followed by birth weight less than 1500 g (25.67%) and cranio-facial anomalies (16.21%). Chou et al. (20) reported that the most common risk factor was the requirement of more than five days of mechanical ventilation (22.4%), followed by chromosomal abnormalities (19.4%), ototoxic drug use (18.5%), birth weight <1500 g (13.4%), familial history of congenital HL (10.3%), postnatal asphyxia (7.3%), sepsis and meningitis (5.2%), cranio-facial anomalies (2.2%), and intra-ventricular hemorrhage (1.3%). In contrast, Mahmoudian et al. (23) reported that the most common risk factor was ototoxic drug use (51.68%), followed hyperbilirubinemia (18.64%).

In our study, a total of 104 newborns (208 ears) underwent the TEOAE test and 23.1% of the right ears and 26% of the left ears failed the test. Moreover, a total of 6.66% of the 60 ears in the healthy group and 31.08% of the ears in the high-risk SNHL group failed the test. Literature indicates that the rate of pathological HL varies between 1.5% and 15%, with the rate varying according to the disease (24).The rate of TEOAE survivors in our study was significantly higher than the general congenital hearing loss rates. This finding may be partly due to the high number of high-risk newborns in the study group, while the underlying factor may be the low sensitivity of the test. Similarly, Mahmoudian et al. (23) compared distortion-product OAE and ASSR and showed

that 27.6% of the right ears and 26.3% of the left ears failed the distortion-product OAE test. Accordingly, the authors recommended re-screening with s-BAER for all infants with a high risk or a failed result (25).

The frequency-specific multiple-ASSR results of all subjects indicated that the rate of failure was higher at low frequencies, whereas it dramatically decreased at high frequencies. Of note, 42.3% of the right ears and 38.5% of the left ears failed the ASSR test at 500 Hz, while the rates of failure were 4.8% and 7.7% at 2000 Hz and 3.8% and 4.8% at 4000 Hz, respectively. Moreover, a comparison of the TEOAE and ASSR results of the subjects indicated that the sensitivity rate increased as the frequency increased, whereby the sensitivity rate was 70.1% at 500 Hz and reached 100% at 4000 Hz. Similarly, the accuracy rate increased at high frequencies and reached the highest rate of 79.81% at 2000 Hz. In the ASSR test, a total of eight ears in the healthy group failed the test at 500 Hz, while all the ears passed the test at high frequencies (2000 and 4000 Hz). In the high-risk SNHL group, however, 50.68% of the ears failed the test at 500 Hz, while only 5.47% of them failed the test at 4000 Hz. In the ASSR and TEOAE measurements in the high-risk SNHL group, the sensitivity and accuracy rates increased and the specificity rates decreased with higher frequencies. ASSR is a periodic electrical response generated in the brain in response to a periodically repeated acoustic stimulus. Since the stimuli are remarkably fast, brain responses result from arousal before the completion of the results of previous arousal, resulting in a steady-state response (12,26). Depending on the modulation frequency, responses are received from different regions in the brain, whereby 40 (range, 35-55) Hz is obtained from the auditory cortex and 80 (range, 70-110) Hz is obtained from brainstem-derived responses (27). The neural sources of responses generated in high-frequency modulations are similar to those of BAER waves (28). In addition, the multiple stimulation in the ASSR causes some kind of functional masking, preventing the neighboring frequency information from responding to the stimulus in the basal membrane of the cochlea, thus providing frequency-specific measurement (10). This feature can be described as physiological recruitment and is likely to allow approaching the behavioral thresholds via multiple-ASSR in patients with cochlear HL (29-30).

In newborns, response amplitudes are small, but they increase gradually throughout the year (31). In particular, since the most significant increase occurs in the first few weeks, changes in behavioral thresholds have been reported in children during the first year (32). In order to eliminate this reduction in signal amplitude, various methods that increase stimulus amplitude or utilize mixed modulation, synchronous signals, and filtering may be used (44).

Numerous studies have shown that at a fast excitation frequency, i.e. high modulation frequency (e.g. 80 Hz), ASSR responses are consistent and reliable in infants (11,33). This has allowed effective use of multiple-ASSR at 80 Hz in the prediction of hearing in infants (30).

Since the response amplitudes are smaller in newborns, their physiological thresholds are higher than those of older children and adults (31,34). Accordingly, the ASSR system enables the estimation of behavioral thresholds from physiological thresholds by creating an estimated audiogram. To achieve this, either the regression or correction approach is used. The device determines the correction factor based on the data obtained from the normal population using one of these approaches with the help of the program. In numerous studies, normal hearing levels for airway ASSR in newborns have been reported as 50 dB at 500 Hz, 45 dB at 1000 Hz, and 40 dB at 2000 and 4000 Hz (8,13,20). In our study, the physiological values obtained in the hearing test were considered "passed" or "failed" based on the statistical analyses.

Mahmoudian et al. (23) compared distraction-product OAE with multiple-ASSR in 118 high-risk neonate s and reported that the ASSR results were highly compatible with those of distortion-product OAE. The authors emphasized that this compliance was stronger in high-frequency ASSR and suggested that ASSR is a safe method for measuring hearing, particularly in newborns at high risk of HL. In our study, hearing was measured with high-frequency ASSR in all newborns and it was observed that the sensitivity of the results was higher at higher frequencies.

In the late 1980s, s-BAER became the most important test used in neonatal hearing screening (35). In Turkey, there are devices of various brands and models used for implementing click t-BAER test. Studies using these devices for determining the thresholds, particularly 2-4 kHz, have reported on a strong correlation between behavioral thresholds (36). However, this method does not provide specific information about the frequencies used in assessment of hearing, and the techniques used for this purpose prolong the test

period. At high modulation frequencies, the characteristics of ASSR are similar to those of clinical BAER, which is another objective technique used in the assessment of hearing. Accordingly, ASSR compensates some of the limitations of click s-BAER.

Comparative studies using BAER and ASSR for the determination of behavioral thresholds have emphasized that the best compliance between these two tests is observed at 2000 Hz. Linares et al. (13) reported that there is a tight correlation between ASSR and click BAER at 2000 and 4000 Hz. Rodrigues et al. (19) also observed and highlighted that the best compliance between ASSR and click s-BAER was found at 1000 Hz and the worst compliance was found at 4000 Hz. In some other studies, the characteristics of BAER were found to be consistent with those of ASSR at 500 Hz (37-39). Nonetheless, there is still no consensus on the frequency that provides the best compliance between ASSR and click s-BAER in determining behavioral thresholds, although it has been reported that the correlation increases with higher frequencies (13,36-39).

In our study, the comparison ASSR and s-BAER in all newborns revealed the highest sensitivity rates at 2000 and 4000 Hz. Although a total of two ears failed in the s-BAER test in the healthy group, all the ears passed the ASSR test at 1000 Hz or higher frequencies. Moreover, although 15.49% of the right ears and 19.71% of the left ears failed in the high-risk SNHL group, these ears obtained their best results in the ASSR test at 2000 and 4000 Hz, whereby only 4.1% of the right ears and 6.8% of the left ears failed the test at 4000 Hz. In the high-risk SNHL group, the sensitivity rates of ASSR and s-BAER were the highest at 2000 and 4000 Hz and the lowest at 500 Hz. This finding is consistent with the findings reported in the literature (32,36-39,40,41). However, Rodriguez et al. (101) reported that the worst compliance between ASSR and s-BAER was observed at 4000 Hz. Turan (42) evaluated the results obtained from hearing-impaired subjects using pure-tone audiometry and ABR and reported on a moderate correlation between the results of ASSR at 500 and 1000 Hz and also noted that the correlation values were higher at 2000 and 4000 Hz. Normal correlation was found to be a low correlation in subjects. This finding contradicted our findings and the authors attributed it to the fact that the study subjects were awake and the testing room was not completely sound-proof. In contrast, many studies have shown a high correlation between ASSR results and pure-tone hearing thresholds (34,35,43).

An important advantage of ASSR is that it provides a prediction of frequency-specific hearing loss as well as compliance with s-BAER in both healthy and high-risk newborns. It has also been shown that ASSR can be used for estimating pure-tone hearing thresholds in infants and young children. In addition, the use of BAER with ASSR is recommended since these two tests complement and support each other (39).

The multi-stimulation technique used in the multiple-ASSR test allows simultaneous evaluation of multiple frequency zones for both ears, enabling rapid and automated testing. This test is time-saving independently from the operator since it evaluates four frequencies simultaneously and eight frequencies in total (45). In our study, average test duration (including preparations) was 30.2±6.45 min for multiple-ASSR. In a similar study, Porto et al. (8) reported that tone-burst ABR and ASSR in terms of duration without considering the pause of the average ABR duration of 21.1 ± 5.5 min, while the average duration of multiple-ASSR was 22 ± 11.1 min. Sininger et al. (3) found that the mean duration of ASSR was 19.93 ± 8.73 min. Mahmoudian et al. [23], in a similar way to our study, reported that the average duration of high-frequency ASSR was 32.99 ± 4.25 min at 40 dB HL and 18.72±4.20 min at 70 dB HL. The authors also noted that frequency-specific thresholds were achieved more quickly through the use of high-frequency ASSR in hearing screening. The importance of the test in a short time will be better understood when there is a risk of waking up from natural sleep at any time (3). In our study, two newborns were awakened after the ASSR measurement and click t-BAER could not be performed in these patients.

Multiple-ASSR is more sensitive in predicting neonatal behavioral hearing status when compared to TEOAE. At higher frequencies, the test provides higher sensitivity and accuracy rates. In addition, the compliance of multiple-ASSR with click-s-BAER was highest at 2000 Hz. Based on our findings, we consider that multiple-ASSR is an objective test that can be used safely in predicting rapid frequency-specific behavioral hearing of bilateral ears simultaneously without requiring practitioner's interpretation, particularly in high-risk newborns. However, further evidence and studies are needed to ensure that the newborn's hearing prediction alone is sufficient.

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