The Prevalence and Causes of Auditory Neuropathy/Dys-synchrony (AN/AD) in Children with Hearing Impairment

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Abstract There are a wide variety of hearing impairments that part of it is auditory neuropathy/dys-synchrony (AN/AD). So, the object of this study was determination the prevalence and causes of AN/AD in children with hearing impairment. This study was a descriptive cross-sectional survey. The sample size consisted of 105 hearing impairment children. All them were under hearing screening tests (tympanometry), distortion and transient evoked otoacoustic emissions (DPOAEs + TEOAE) and automated auditory brainstem response (AABR). If they were suspected to AN/AD, for complete diagnostic measurements were referred to our hospital. Four cases (8 ears) with AN/AD were diagnosed, which had an average age 37 months (SD = 8.67). So, the prevalence of AN/AD was 3.8 % among hearing impaired children. The findings of this study showed that there are the relationships between AN/AD and fluctuating hearing loss, acoustic reflex, high bilirubin, blood exchange after birth, neonatal intensive (NICU) care unit ($P < 0.05$). The simultaneous use of both ABR and OAE tests in the birth screening provide much

more useful information than when each of these tests is used alone.

Keywords Auditory neuropathy · Auditory brainstem responses · Distortion product otoacoustic emissions · Transient evoked otoacoustic emissions

Introduction

In patients with AN/AD, the function of the external hair cells of the cochlea is normal, while the neural conduction at the level of the vestibulo-cochlear is damaged. In this regard, the responses of otoacoustic emissions (OAE) are normal and there is abnormality in brainstem response [1–3]. For this reason, children and infants with this neurological disorder are not detected using OAE. Because, it only examines hearing to the earliest level of the ear or the hair cells of the cochlea and this lack of identification causes a wide range of the problems, including language, communication and educational difficulties [4, 5]. Since, primary detection of these patients is very effective in rehabilitation and instruction, early identification and intervention of these individuals is essential [6].

The term of AN/AD was first proposed in the 1980s, following the observation of the patients with normal pure tone thresholds, which had difficulty to detect the sounds, especially in a noisy environment. AN/AD was identified in the pediatric population by initiating neonatal hearing screening [3, 6, 7].

The location of the lesion in auditory neuropathy includes internal hair cells, auditory nerve fibers, auditory neurons in the spiral ganglia or a combination of these. It is

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also possible that the pathways of the afferent nerve are involved, such as the pathway of the efferent [5–7].

The pure tone audiogram in these subjects is in the range of normal to profound hearing loss and based on most findings had low tone hearing loss pattern. Acoustic reflexes are not present in these people and their recognition scores are much weaker than what is expected on the loss of their pure tone audiogram [1, 6, 7]. So, the object of this study was determination the prevalence and causes of AN/AD in children with hearing impairment.

Materials and Methods

The contract for this project was signed by our university on February 2015 and number 9311145893. This study was a descriptive cross-sectional, which done from February 2015 to February 2017 at our center. The Population studied consisted of 105 hearing impairment persons (girls and boys of our rehabilitation center and deaf school) with a minimum of 8 months and a maximum of 18 years. The subjects were volunteers and all their parents received detailed information about the study and testing that would be involved.

The exclusion criteria were age more than 18 years. The cases who had cochlear implantation. The abnormality in the ear helix and external auditory canal. The abnormal tympanic membrane and tympanograms (Type B, Type C).

The inclusion criteria consisted of the age range 8 months to 18 years, intact tympanic membranes, the lack of middle and the external ear problem and normal tympanogram (A). The criteria for AN/AD was the normal findings of the one or the both OAE responses, with abnormal ABR results and no acoustic reflexes [3, 4].

Ethical considerations: In this research, privacy and personal information were reserved and respected. There was no action that was in conflict with their safety, health and well being, and they were excluded from the survey at any stage that the individuals concerned were reluctant to continue to cooperate.

Assessments

The steps for the practical work that was in the beginning: all the children were by the hearing screening tests (tympanometry, TEOAE, DPOAE, AABR). If a problem was observed in the middle ear, the child was referred for medical examinations. The re-test was performed after 4–6 weeks and if we did not see the recovery, the child was excluded from our study. When, the auditory neuropathy in childhood was suspected, they were referred to our hospital for complete evaluation. After initial full examinations and history taking by our otolaryngologist, full auditory battery

test consisted of IA, DPOAE, TEOAE, PTA, speech tests (for older than 4 years or for the younger children who participated in the test) and ABR were performed.

In every morning, checking calibration was done to ensure that all instruments produced at the specified level and frequency. Also, during the process, we ensured that the persons were attended to their task. In each step of evaluation, when the procedure was completed for the one test, subjects were given a short break and the whole procedure repeated for another.

For the impedancemetric tests, middle-ear pressures and acoustic reflex measurements were made using Interacoustics MAICO MI34 impedancemeters and TDH-39 earphones. The middle-ear pressure between the limits of ± 50 dapa was evaluated. The values that were out of this limit were omitted from the analyses [8].

Distortion Product Otoacoustic Emissions (DPOAEs) was measured (Labat Epic-plus). The f1/f2 ratio fixed at 1.22, and stimulus levels were held constant at L1 = 65 dBspl and L2 = 55 dBspl. The 2 f1–f2 DPOAE amplitudes were recorded at frequencies (f2) 1.0, 1.5, 2.0, 3.0, 4.0, 6.0, and 8.0 kHz. The DPOAE amplitudes were considered significant when they were at least 3 dB above the noise floor. The averaged values less than 3 dB were omitted from the analyses [9].

Transient evoked otoacoustic emission measurement was conducted with a transient evoked (TE) full menu. The eliciting stimuli were conventional, nonlinear clicks of 80-microsecond duration, delivered at a peak sound pressure level of $83 + 3$ dB. The signal-to-noise ratio in at least three of the five highest frequency bands (i.e., 1, 2, 3, 4 and 5 kHz) exceeded 3 dB [9]. All subjects older than 4 years underwent pure tone hearing threshold assessments between 250 and 8000 Hz. Air and bone conduction hearing thresholds and speech tests were conducted within sound proof rooms, using an MADSEN (OB822, Denmark).

Subjects' air conduction hearing thresholds were measured, using standard earphones (TDH-39) at 250–8000 Hz. Bone conduction hearing thresholds were measured using 60,273 vibrators (Oticon, Denmark) at 0.5–4 kHz. Audiometers were calibrated using 4152 artificial ears with a Larson Davis (U.S.) sound level meter.

Subjects' speech reception thresholds were assessed using a two-syllable word list. Speech recognition was tested using a monosyllable, phonetically balanced word list developed in our university. The uncomfortable loudness level was also determined.

Auditory brainstem response to the click stimulation (ABR) were tested (Labat Epic-plus). With noninverting electrode placed at the high forehead and inverting electrode on ipsilateral mastoid and ground electrode on contralateral. Electrode impedances were roughly equivalent

and were < 5 kilohms at the start of the test. Responses to 2000 stimuli were averaged (rate of 11.1/s. Responses were filtered from 70 to 3000 Hz (10).

Data Analyses

All analysis was done by means of the statistics software SPSS₁₇. Data were expressed as mean $\pm$ standard deviation. Kolmogorov–Smirnov test was used for evaluation of normal test distribution. Fisher's exact test used to compare findings among cases. *P* value of < 0.05 was considered to indicate statistical significance.

Findings

In this study, from the 105 children who underwent tympanometric evaluation at the beginning of the survey, 8 cases had abnormal tympanograms, which were referred for medical treatment and were excluded from the study. Therefore, our study population was 97 (194 ears) and ABR + OAE tests were performed on this group. Four cases (8 ears), which included a boy and three girls with AN/AD were diagnosed, which had an average age 37 months (SD = 8.67). Two children (4 ears) did not have TEOAE, but the DPOAE response was recorded. In two other cases (4 ears), the TEOAE and DPOAE were recorded as normal. So, rejection rate based on TEOAE was 2.06% and the acceptance rate was 97.94%. However, the acceptance rate based on DPOAE was 100%. All four had no acoustic reflexes. In the audiometric test of pure tone, one of the four subjects (2 ears) had severe hearing loss and three others (6 ears), moderately to severe. Of the 4 children diagnosed with auditory neuropathy, two of them had hyperbilirubin at the birth, with one having a history of blood transfusion and another had a history of oxygen deficiency. None of them had a history of Perinatal asphyxia.

So, the prevalence of neuropathy was 3.8 % among hearing impaired children. The findings of this study showed that there are the relationships between auditory neuropathy and fluctuating hearing loss (Table 1), acoustic

reflex (Table 2), high bilirubin (Table 3), blood exchange after birth (Table 4), neonatal intensive care unit (Table 5). Also, all differences are significant (*P* < 0.05).

In addition, according to records from the center of cochlear implant in our hospital was observed that four children had cochlear implant prostheses with a history of preoperative history of neuropathy. However, due to the fact that the TEOAE test was not conducted for this group of children, they did not enter the study.

Discussion

AN/AD in patients with heterogeneous clinical symptoms indicate different etiology, like high bilirubin, prematurity, ototoxic drugs, anoxia, asphyxiation, cerebral palsy and infections [7]. In the spectrum of AN/AD disorders, the transmission pathway from the peripheral to the central part is difficult and those who suffer from this disorder have problems such as speech impairment especially in the presence of noise and the development of linguistic skills [8, 9].

Patients with this abnormalities have normal function in external hair cells and abnormal function in the cochlea-to-brain pathway. As a result, the response of the cochlear microphonics and OAE test is normal, but due to the lack of neural synchrony, the brain stem response (ABR) is absent or highly abnormal [10].

Although the prevalence of AN/AD is not specified exactly, but there is a hypothesis that the prevalence of the disorder in the sensory-neural hearing impairment subjects is of 0.2 to 15% [3, 6, 7].

In this case, otoacoustic emission (OAE) result is normal and there is no ABR response, and if detectable, it is abnormal [11]. There is a wide range of hearing loss in people with neuropathy and varies from mild hearing loss to complete deafness [12]. In this study, 97 hearing impaired children (194 ears) were evaluated. Four children with bilateral AN/AD (8 ears) were identified. In these four cases, a boy was a boy and three children were girls. Risk factors related to auditory neuropathy include high bilirubin, oxygen deficiency, NICU unit, genetic disorders, birth

Table 1 Relationship between auditory neuropathy/dys-synchrony (AN/AD) and fluctuating hearing loss in children with hearing impairment (n = 8 ears)

Fisher's exact test	Fluctuating hearing loss		Auditory neuropathy
	No	Yes	
<i>P</i> < 0.001	6	2	Yes
	194	0	No

Relationship between auditory neuropathy and fluctuating hearing loss

Table 2 Relationship between auditory neuropathy/dys-synchrony (AN/AD) and acoustic reflex in children with hearing impairment (n = 8 ears)

Fisher's exact test	Acoustic reflex		Auditory neuropathy
	No	Yes	
$P < 0.001$	8	0	Yes
	152	42	No

Relationship between AN/AD and acoustic reflex

Table 3 Relationship between auditory neuropathy/dys-synchrony (AN/AD) and high bilirubin in children with hearing impairment (n = 8 ears)

Fisher's exact test	High bilirubin		Auditory neuropathy
	No	Yes	
$P < 0.013$	4	4	Yes
	174	20	No

Relationship between AN/AD and high bilirubin

Table 4 Relationship between auditory neuropathy/dys-synchrony (AN/AD) and blood exchange after birth in children with hearing impairment (n = 8 ears)

Fisher's exact test	Blood exchange after birth		Auditory neuropathy
	No	Yes	
$P < 0.05$	6	2	Yes
	186	8	No

Relationship between AN/AD and blood exchange after birth

Table 5 Relationship between auditory neuropathy/dys-synchrony (AN/AD) and a history of hospitalization in neonatal intensive care unit (NICU) in children with hearing impairment (n = 8 ears)

Fisher's exact test	Neonatal intensive care unit		Auditory neuropathy
	No	Yes	
$P < 0.008$	4	4	Yes
	176	18	No

Relationship between AN/AD and a history of hospitalization in neonatal intensive care unit

defects, and pregnancy problems. Based on the present study, the association between AN/AD and factors such as hospitalized in newborn, or neonatal, intensive care unit (NICU), high bilirubin, and problems during pregnancy were statistically significant ($P < 0.05$). Two out of four people diagnosed with AN/AD had neonatal jaundice. One has a history of transfusion. In one of these four children, there was a risk factor for oxygen deficiency (anoxia). In 50% of the cases of AN/AD, one or all of the above factors were reported, which was consistent with the authors [13–15].

In the present study, there was no relationship between the duration of pregnancy and auditory neuropathy, because the duration of pregnancy in all 4 children with AN/AD was 9 months. There was also no significant relationship between AN/AD and pregnancy problems. Only, one of these four children did not have this risk factor. The results of the studies showed that risk factors such as pre and postnatal birth problems (preterm birth and weight less than 1500 g) were observed in some people with neuropathy [16]. In a study was found that 87% of people with AN/AD have a history of hearing loss with a

genetic basis. Also, 62% of the subjects had neonatal risk. Also, there were factors in people with risk factors such as high bilirubin, meningitis, anoxia, auto-toxic drugs, infection and familial history [17]. In the study of Talaat et al., which was done on the affected children to the AN/AD, they found that 40% of patients had hyper bilirubin level, 13.3% had oxygen deficiency and 46.7% of patients had no specific disease history. In a study, which was on the patients in NICU, were observed that in comparison with normal children, there is the predisposition factors for AN/AD children, such as IRDS, meningitis and the use of vancomycin [4]. These results are consistent with our study. Of course, it should be noted that a significant percentage of children with AN/AD do not have any of the risk factors associated with the disease. So, It seems that the screening is not only enough in infants with risk factors and all battery approach tests for diagnosing is necessary.

In our research, the prevalence of neuropathy was 4.12% among hearing impaired children and we did not use an electrocochleography test to evaluate the cochlear function. It seems that using this test, the prevalence of AN/AD is higher and exactly. To identify people with AN/AD, both cochlear microphonic test and otoacoustic emissions can be used to evaluate the function of the cochlear cells. However, the results of these two methods are not always the same.

The cochlear microphonic can be detected when auditory otoacoustic emissions is not detectable. It can be recorded in people who are infected. Different interpretations can be made for this lack of matching results, including the possibility of partial involvement of the middle ear and consequently [18], the absence of recording of otoacoustic emissions or significant damage hair cells [2].

Conclusion

We concluded that performing a cochlear-sensitive auditory test (OAE) and the auditory brain stem response (ABR) is necessary for the early diagnosis of AN/AD. The use of the DPOAE test for the diagnosis of AN/AD has a significant effect, and in the first stage of screening, the AABR test is recommended.

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Compliance with ethical standards

Conflict of interest Authors declare that they have no conflict of interest.

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