Aud Vest Res (2015);24(2):104-109.

RESEARCH ARTICLE

Evaluation of auditory brainstem pathways in neonates with respiratory distress syndrome

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Received: 25 Jan 2015, Revised: 27 Feb 2015, Accepted: 9 Mar 2015, Published: 25 Mar 2015

Abstract

Background and Aim: Respiratory distress syndrome (RDS) is a lung disorder, which can damage the auditory brainstem pathways because of hypoxia. The aim of this study was to evaluate brainstem auditory electrophysiology changes of neonates with RDS.

Methods: fifteen term neonates who suffered from RDS, 15 term neonates admitted in the NICU for any reason except RDS, and 15 normal term neonates as control group were studied from June to November 2014. Auditory brainstem response (ABR) was recorded by clicks, delivered at 80 dBnHL, the polarity was alternative, the band pass filter and the time window were 50-2000 Hz and 15ms with total 2000 sweeps, respectively. Data were analyzed by ANOVA and paired t-test using SSPS18.

Results: The absolute latencies of waves I, III, V and I-III, I-V intervals of both ear in RDS group and the participants admitted in NICU were significantly longer than controls (p=0.00).

Conclusion: Hypoxia and asphyxia due to RDS can damage the auditory brainstem pathways in neonatal period; additionally, the neonates who were admitted in NICU are also at the risk of auditory brainstem deficit. The findings shed light on the importance of assessing the auditory brainstem function in neonates who had RDS and who were admitted in NICU.

Keywords: Neonate; respiratory distress syndrome; auditory brainstem response; neonate intensive care unit

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Introduction

Respiratory distress syndrome (RDS) is a life-threatening lung disorder in which a baby's lungs are not fully formed and cannot function outside the uterine. RDS is one of the most common causes of neonatal respiratory failure and neonatal mortality which is caused by developmental insufficiency of surfactant production and structural immaturity in the lungs [1]. Labored breathing which is characterized by grunting, nasal flaring and the use of accessory muscles of respiration, arterial hypoxemia and anoxia is the most common clinical sign of RDS. This disease is categorized in to three levels of mild, moderate and severe [2]. The diagnosis of RDS is usually based on clinical manifestation, arterial blood gas analysis and chest X rays [1]. According to studies, it seems that there is statistical correlation between cesarean and respiratory distress syndrome [3].

The neonates who have lung disease and receive oxygen are at the risk of neurological damage [4]. The histology studies revealed that perinatal asphyxia and arterial hypoxia lead to damage of central auditory pathways. These deficiencies including loss of neurons with gliosis or ischemic cell changes in the cochlear nuclei, superior olive and inferior colliculus; also it is well known that severe hypoxemia disturb the metabolism of neurons and depress the electrophysiological function of synapses. Like other central nervous systems (CNS), the central auditory system is sensitive to hypoxemia. It is hypothesized that the hypoxemia associated with neonatal RDS may also affect the central auditory system [4,5,6].

The auditory brainstem evoked response (ABR) is a non-invasive and objective test that reflects functional integrity and development of the brainstem auditory system. This test consists of seven waves that the most important of them are I, III, V waves. The V is the most consistent wave that is most used in clinical practice [7].

The study of Martinesa et al. revealed that the neonate who suffers RDS and hyperbillirubinemia together statistically has been failed in automatic auditory brainstem response (AABR) and has sensory neural hearing loss but the neonate who has only RDS has not been failed statistically in AABR [8].

Coenraad et al. showed that among neonates who admitted to the NICU, the neonates with RDS and meningitis who have been administered vancomycin for a long time, statistically have abnormal ABR waves and they are more susceptible to have auditory neuropathy [9]. In the study of Jiang et al. the latency of wave V and inter-peak latency of I-V increased in neonates with chronic lung disease, but the latency of wave III and inter-peak latency of I-III was in normal limit, so it revealed that apparently, major impairment in neural conduction in the central regions of the brainstem are more than peripheral regions [10].

Because of controversial results in the probable influence of respiratory distress syndrome on auditory brainstem pathways, the aim of this study was to evaluate the auditory brainstem pathways in neonates with respiratory distress syndrome.

Methods

The current cross-sectional study was conducted in Audiology Clinic, Tehran University of Medical Sciences, Tehran, Iran, from June to November 2014. Participants are divided into 3 groups. Group 1 is comprised of 15 term neonates (7 males and 8 females) who had only moderate RDS which was diagnosed by pediatrician according to chest radiography and blood test. In group 2 there are 15 term neonates (6 males and 9 females) who had been admitted in NICU for up to 10 days due to any reason except RDS, and group 3 is comprised of 15 term normal neonates (9 males and 6 females) as the control group. The entrance criteria for all A_n type tympanogram groups are the presence of ipsilateral acoustic reflex and the pass result in transient otoacousticemission (TEOAE) test to rule out ear problems. Also the neonates and their mothers during the pregnancy should not take ototoxic drug.

At first, each neonate was examined using otoscopy, then immitance audiometry Zodiac 901 was performed (Madsen, Denmark). Afterwards, TEOAE was administered (MAICO, by Madsen, Denmark), finally ABR with ICS CHATER (Madsen, Denmark) was recorded. The neonates were slept on bed in calm situation while the non-inverting electrode was placed on their forehead (the electrode array was ipsi-vertical), the reference electrode was placed on mastoid of stimulus site and the ground electrode was on the other mastoid. The acceptable electrode impedance was 5 k Ω. The 100μs click stimuli was delivered by insert earphone at 80 dBnHL. The polarity was alternative, the band pass filter and the time window were 50-2000Hz and 15ms with total 2000 sweeps, respectively. The presentation of stimuli was accidental to each ear. The variables in this study were the latency of waves, I, III, V and the inter-peak latencies (IPL) of I-III, I-V, III-V.

The SPSS18 was used to analyze the data and p-values of ≤0.05 considered to be statistically

Table 1. Mean absolute latencies (ms) and standard deviation of ABR waves in three groups

	Group1		Group 2		Group 3	
Absolute latencies of waves	Right ear	Left ear	Right ear	Left ear	Right ear	Left ear
I	1.97 (0.2)	1.94 (0.19)	2.05 (0.16)	2.04 (0.18)	1.56 (0.22)	1.55 (0.26)
III	4.80 (0.19)	4.83 (0.22)	4.96 (0.28)	4.90 (0.2)	3.98 (0.17)	4.07 (0.19)
V	7.06 (0.23)	7.07 (0.26)	7.18 (0.19)	7.17 (0.2)	6.18 (0.24)	6.23 (0.26)

significant. To assess the normality of data the Kolmogorov–Smirnov test was performed. To compare the absolute and inter- peak latencies among 3 groups the ANOVA test was employed, to compare absolute and inter- peak latencies between ears in each group paired sample t-test was used.

Results

In the controls, the mean latency of wave V in the right and left side were 6.18 (SD=0.24ms) and 6.23 (SD=0.26ms), respectively. In group 1, the mean latency of wave V in the right and left side were 7.06 (SD=0.23ms) and 7.07 (SD=0.26ms), respectively. In group 2, the mean latency of wave V in the right side and left were 7.18 (SD=0.19ms) and 7.17 (SD=0.20ms), respectively. Data analysis revealed no significant differences between the mean I, III and V latency of right and left side in each group (in control group 1 p=0.242, p=0.134, p=0.106 in waves I, III and V latency respectively, in group 1 p=0.182, p=0.210, p=0.68 in waves I, III and V latency respectively, group 2 p=0.54, p=0.15, p=0.35 in waves I, III and V latency respectively).

The absolute latencies of waves I, III, V of both ear in group 1 and 2 were longer than controls and these differences were statistically significant (p=0.00), but there was no significant difference between group 1 and 2 (p=0.46, p= 0.12, p= 0.71 for waves I, III and V respectively). Table 1 shows the mean absolute latencies of waves in each group.

In control group, the mean inter-peak interval of I-V in the right and left side were 4.60 (SD=0.28ms) and 4.65 (SD=0.32ms), respectively. In group 1, the mean inter-peak interval of I-V in the right and left side were 5.04 (SD=0.15ms) and 5.13 (SD=0.17ms), respectively. In group 2, the mean inter-peak interval of I-V in the right and left side were 5.08 (SD=0.16ms) and 5.08 (SD=0.18ms), respectively. Data analysis revealed no significant differences between the mean I-III, III-V and I-V inter-peak interval of right and left side in each group (in control group p=0.34, p=0.95, p=0.29 in interval waves I-III, III-V and I- V latency respectively, in group 1 p=0.102, p=0.42, p=0.13 in interval waves I-III, III-V and I- V latency respectively, group 2, p=0.48, p=0.23, p=0.96 in waves I, III and V latency respectively).Table 2 shows the mean interval of all latencies in each group.

Statistical analysis showed I-V and I-III inter-peak interval of both ears in group 1 and 2 were significantly longer than control group (p=0.00), but there was no significant difference between group 1 and 2 (P=0.79 in I-III inter-peak interval and p=0.83 in I-V inter-peak interval). In group 1 and 2 the III-V interval was slightly longer than group 3, but these differences were not significant (p= 0.713). Figures 1, 2 and 3 show the sample of the waves in each group.

Discussion

The aim of this study was to evaluate the auditory brainstem pathways in neonates with RDS. Our study revealed the general changes in brain-stem auditory electrophysiology in neonates who had RDS during the neonatal period. The present study revealed that the wave I, III and V latencies were longer in participants who had RDS than normal group. These

Table 2. Mean interval latencies (standard deviation) of ABR waves in three groups

	Group1		Group 2		Group 3	
Absolute latencies of waves	**Right ear**	**Left ear**	**Right ear**	**Left ear**	**Right ear**	**Left ear**
I-III	2.80 (0.14)	2.87 (0.12)	2.84 (0.16)	2.82 (0.16)	2.40 (0.22)	2.44 (0.27)
III-V	2.25 (0.22)	2.23 (0.18)	2.21 (0.14)	2.27 (0.14)	2.19 (0.19)	2.19 (0.22)
I-V	5.04 (0.15)	5.13 (0.17)	5.08 (0.16)	5.08 (0.18)	4.60 (0.28)	4.65 (0.32)

significant increases in wave latencies reflect that hypoxemia in RDS participants can damage the central auditory pathways system. Auditory neurons in the neonatal brainstem are vulnerable to hypoxic-ischaemic and the most likely major risk for neurological impairment and developmental deficits. It is probable that severe hypoxia and hypoxia-ischaemia can disturb the metabolism of neurons and depress the electrophysiological functions of synapses that transmit developmental as well as regulatory signals between neurons. This can result in neuronal impairment [7,8]. Findings of this study are in agreement with the study of Jiang et al. which revealed that latency of waves I, III and V increase in neonates who suffer hypoxic-ischaemic due to chronic lung disease and perinatal asphyxia; that is apparently the result of damage of the central auditory system. Additionally, waves I, III and V latencies in participants who were admitted in NICU for any reason other than RDS, were longer than the control group and there were statistically significant differences between them.

This is in agreement with the study of Jiang et al. which revealed that the high-risk neonates, who were admitted in NICU, demonstrated a significant abnormal increase in ABR variables including wave V latency, III-V and I-V inter-peak intervals; that mainly reflect more central function of the brainstem auditory pathways.

The intervals of I-III and I-V in RDS participants were significantly longer than normal group. This may be mainly related to the hypoxia associated with neonatal RDS that affects myelination of the central auditory pathways. This is inconsistent with the Strata et al. study, that the interval latencies increase significantly in rat which had perinatal anoxia [13] and also it was in agreement with the study of Jiang et al. in which I-V, I-III and III-V intervals increase in term neonates who had asphyxia [8]. This suggests that asphyxia, hypoxaemia and perinatal anoxia can directly damage the auditory system, and indirectly affect the system by cardiovascular collapse and cerebral ischaemia, resulting in an acute impairment in auditory neural pathways [8]. The intervals of I-III and I-V intervals also were significantly longer in neonates who were admitted in NICU than normal group. The intervals of I-III, III-V and I-V did not show any difference between group 1 and 2. It seems that brainstem function is impaired similarly in neonates who had RDS and who were admitted in NICU, and that the two clinical situations exert a similar effect on functional integrity of the brainstem.

The results of this study indicate that infants who suffer RDS and were admitted in NICU are in risk of auditory brainstem deficit. Hypoxia in RDS participants affects functional integrity and development of the brain [12]. In both human infants and experimental animals, brainstem auditory neurons are shown to be particularly sensitive to severe hypoxemia, chronic and sublethal hypoxia, which may result in severe impairments in corticogenesis in the developing brain and a significant decrease in subcortical white matter [12].The significant increase in waves I, III and V latencies and intervals indicates that RDS, the damage due to hypoxic-ischaemic, asphyxia and anoxia insult to the central auditory system. This insult interferes

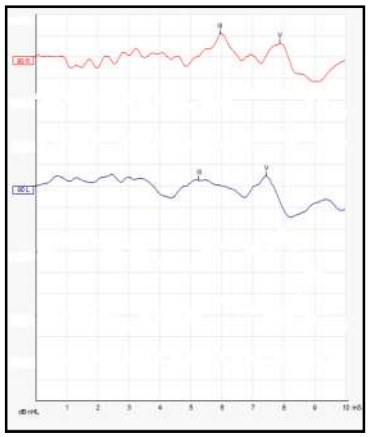

Fig. 1. A sample of ABR waves in infant with respiratory distress syndrome.

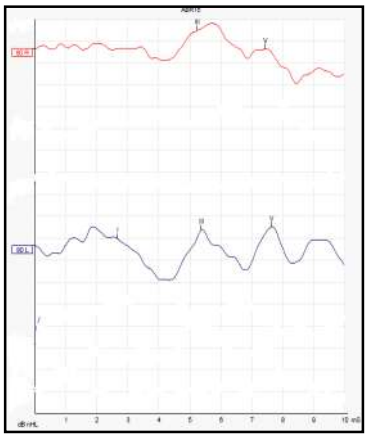

Fig. 2. A sample of ABR waves in neonate admitted in NICU.

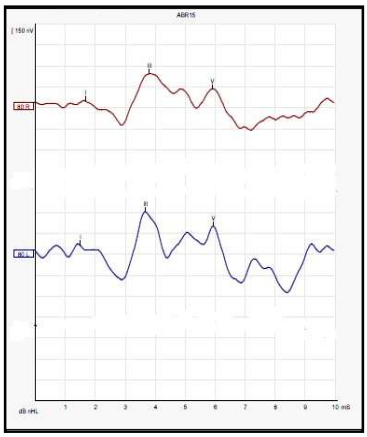

Fig. 3. A sample of ABR waves in an infant in control group.

with nerve conduction which is related to myelination and synaptic transmission of the neonatal auditory system. Also according to increase the wave I latency and I-III interval we can suggest that RDS can damage peripheral auditory system too.

Conclusion

Our data suggest that neonates who had RDS are at the risk of auditory brainstem pathways deficit because of hypoxia and asphyxia that have occurred in RDS participants. Also the neonates who were admitted in NICU are at the risk of auditory brainstem deficit too. These findings shed light on the importance of assessing the auditory brainstem function in neonates who had RDS and who were admitted in NICU.

Acknowledgements

This article is emerged from M. Sharifinik MSc. dissertation in Audiology submitted in Tehran. The research has been supported by Tehran University of Medical Sciences grant number 260/1086.

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