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Comparison of Ce-Chirp Impulse Latency and Amplitude Values Between High Risk Prematures with Corrected Age of 0-6 Months and Healthy Newborns

Düzeltilmiş Yaşı 0-6 Ay Arası Yüksek Riskli Prematürelerde Ce-Chirp Uyaran Latans ve Amplitüd Değerlerinin Sağlıklı Yenidoğanlarla Karşılaştırılması

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This study was presented as an oral presentation at the 6th National Otology Neurotology Congress, 28 April-1 May 2018, Antalya, Turkey.

ABSTRACT Objective: The obtained mean latency and amplitude values will help us for clinical interpretation of high risk prematüre infants and newborns' ABR tests by using ce chirp impulse. **Material and Methods:** In this study, 35 high-risk premature and 35 healthy newborns with a corrected age range of 0-6 months were included. The wave latency and amplitude values in the auditory brainstem response (ABR) test of 500, 1000, 2000 and 4000 Hz using the narrow-band chirp stimulus were compared in these two groups. **Results:** V-wave values obtained from all infants were obtained at the highest amplitude (0.58 μV) at 90 dB at 1000 Hz and the shortest latency (3.73 ms) at 90 Hz at 2000 Hz in healthy newborn. There was no significant difference between V wave latencies with regard to gender. In our study, as a result of V wave latency and amplitude measurements obtained in comparison of high-risk premature and healthy newborns, a statistically significant difference was found between all frequencies (500, 1000, 2000 and 4000 Hz) and narrowband chirp stimulus between the two groups. **Conclusion:** Considering that auditory neural maturation persisted up to 18 months, we obtained mean values that will help clinical interpretation of high-risk premature infants and newborns by using the V wave latency and amplitude values.

Keywords: Newborn; auditory brainstem response; premature

ÖZET Amaç: Belirlenen latans ve amplitüd değerleri, yüksek riskli prematürlerde ve yenidoğanlarda yapılacak ce chirp uyaranlı ABR ölçümlerinin değerlendirilmesinde yardımcı olacaktır. **Gereç ve Yöntemler:** Bu çalışmada işitme kaybı şikayeti olmayan ve otoskopik muayenesi normal olan, düzeltilmiş yaşı 0-6 ay arası 35 yüksek riskli prematüre, 35 sağlıklı yenidoğan olmak üzere iki grupta bulunan toplam 70 bebeğin 500, 1000, 2000 ve 4000 Hz'deki ve dar bant chirp uyaran kullanılarak yapılan işitsel beyin sapı cevabı (İBC) testindeki dalga latans ve amplitüd değerleri karşılaştırılmıştır. **Bulgular:** Tüm bebeklerden elde edilen V. dalga değerlerinde en yüksek amplitüd (0,58 μV) 1000 Hz'de 90 dB şiddetinde, en kısa latans (3,73 msn) 2000 Hz'de 90 dB şiddetinde sağlıklı yenidoğanda elde edilmiştir. Cinsiyetlere göre yapılan değerlendirmede V. dalga latansları arasında anlamlı fark bulunmamıştır. Çalışmamızda yüksek riskli prematüre ve sağlıklı yenidoğanların karşılaştırılmasında elde edilen V. dalga latans ve amplitüd ölçümleri sonucunda tüm frekanslarda (500, 1000, 2000 ve 4000 Hz'deki) ve dar bant chirp uyaran ile iki grup arasında istatistiksel olarak anlamlı faklılık bulunmuştur. **Sonuç:** Sonuç olarak işitsel nöral matürasyonun 18. aya kadar devam ettiği dikkate alındığında, çalışmamızda elde edilen V. dalga latans ve amplitüd değerlerinin yüksek riskli prematüreler ve yenidoğanlara ait klinik yorumda yardımcı olacak ortalama değerler elde edilmiştir.

Anahtar Kelimeler: Yenidoğan; işitsel beyinsapı cevabı; prematür

The neurological auditory pathway starts from the spinal ganglion in the cochlea and extends to the auditory cortex in the temporal lobe. A stimulus given as sound energy to the external ear canal is converted into the electrical stimulus by the cochlea and reaches the auditory cortex approximately in one-third of a second.

Stimuli used to obtain auditory stimulation potentials are divided into 3 groups according to frequency bands; Click stimulus (includes the whole frequency band), Tone-Burst stimulus (including a narrow frequency band) and chirp stimulus. The auditory brainstem response (ABR) thresholds obtained by the stimulus indicate that the high frequency region (part of the cochlea between 2000-4000 Hz) reflects the activation and does not provide information for frequency.[1,2] Additionally, click stimuli in turn stimulate the cochlea from the apex to the basal fold of the basilar membrane. This is called the "cochlear travel delay" (the circulation period of the sound wave in the cochlea). The tonal stimulus is frequency-specific and gives information about the hearing at the frequencies used as stimulus. Tonal stimuli are used to obtain frequency-specific ABR thresholds. This type of sound stimuli is called tone-burst. An ideal "tone burst" to generate an audible stimulus should consist of only one frequency and maintain energy density at that frequency. In this way, only the desired frequency region of the cochlea is stimulated. However, in this implementation a good balance between the duration of the tone-burst stimulus and the precision of its frequency should be created. Very short-time stimuli cause cochlear stimulation at frequencies other than the original frequency of the stimulus, "called frequency" scattering.[3] When longer, but very high amplitude stimuli are used, it stimulates all the frequency areas of the cochlea and the response obtained is not frequency-specific. For this reason, notch noise, linear and non-linear windows are used to reduce the participation of side frequencies.[4] The latency values and appearance of tone burst ABR are different from those of click ABR. Latency in tone burst ABR is longer due to long wave time along the basal membrane and increased output time of the stimulus.[5]

Chirp stimuli compensate for the cochlear travel delay to provide neural synchronization and large amplitude responses. Chirp stimulus can be used as broadband or as a frequency-specific narrow band. The aim is to deliver each frequency component to the corresponding region within the cochlea at the same time and to obtain the maximum amplitude response. Auditory brainstem response recordings generated by the chirp stimulus show amplitude waves greater than 1.5-2 times larger, especially at low intensities (20-40 dB) compared to click stimulus.[6]

MATERIAL AND METHODS

This study was performed at the Department of Audiology Speech Voice Disorders in the Ear-Nose-Throat Department of Baskent University in Ankara. It was approved by the Board of Ethics of Başkent University on 24.10.2014 with the decision number of 14/122.

Since participation in the study is voluntary, the parents of all newborns included in the study have signed a document with "Başkent University Clinical Research Ethics Committee Informed Volunteering Form for Scientific Research in Children".

This study consisted of 70 patients (35 women, 35 man) with a normal external ear canal and tympanic membrane in otoscopic examination.

For healthy newborns, it was taken into consideration that the birth week was 35 weeks and above, the birth weight was 1500 g and above and inclusion criteria included, the lack of consanguineous marriage, the lack of genetic disease, and absence of any disease that would affect hearing before and during the test.

The diagnosis of high risk preterm births (corrected age of 0-6 months) was based on the criteria established by the Joint Committee on Infant Hearing 2007 guidelines.[7]

These criteria include;

- Low birth weight (1500 g and below)
- Consanguineous marriage and hereditary hearing loss in the family
- Prenatal infection
- Birth week (35 weeks and below)
- Blood transfusion or hyperbilirubinemia higher than 15
- Mechanical ventilation lasting more than 10 days
- Intensive care unit than stay longer 5 days.

Before the ABR tests; routine otorhinolaryngology examinations were performed, and those whose normal appearance of the eardrum were taken to the next stage. All babies were administered Transient Evoked Otoacoustic Emissions (TEOAE) and all passed.

The Interacoustics Eclipse Smart EP25 clinical ABR system (Interacoustics A/S, Middelfart, Denmark) was used for ABR recordings.

CE-Chirp stimuli were used in the recording parameters as a stimulus rate of 11.1/sec high-risk premature infants and a rarefaction polarity with recurrence frequency for healthy newborns. A frequency range of 30 msec for the recording window and 50-3000 Hz for the recording filter was selected, and 1500 samples were collected at each intensity level. Four single-use Ambu Blue Sensor N EEG Of the electrodes, were used for each recording. Electrodes; the ground line was placed on the cheekbone, the positive line was placed on the upper part, one of the negative electrodes on the left ear mastoid and the other one on the right ear mastoid. During the test, care was taken to ensure that the cables were as far away from the recording device as possible, not to overlap, and the electrode impedances were below 5 Ωk during recording. During the study, ER-3A (Etymotic Research) headphones were used. In our study, V wave latency and amplitude values were measured with CE-Chirp stimulus which was sent at 90, 70, 50, 40 and 20 dB intensities at 500, 1000, 2000 and 4000 Hz respectively. The latency and amplitude values measured at each level of severity were compared for the high-risk premature and healthy newborns with gender, right and left ear values.

STATISTICAL ANALYSIS

Data were analyzed by SPSS 21.0 package program. Continuous variables were given as mean±standard deviation, median (minimum-maximum values) and categorical variables as number and percentage. Because the data had a normal distribution, the analyses were conducted using parametric tests. The average values of numeric data were calculated with the Student's t-test and the variables with non-normal distribution were evaluated with the Mann-Whitney U test. Wilcoxon test was used to determine the difference in mean of two samples. Regarding the comparative assessments, the accepted limit of significance was $p<0.05$.

RESULTS

In this study, in order to obtain ABR CE-Chirp stimulus latency and amplitude data in 35 healthy newborns and 35 high risk prematures. The gender distribution of the babies included in the study was grouped as shown in Table 1. The distribution of babies according to the birth week and birth weights of babies in Table 2.

1. Gender distribution of babies participating in the study

2. Distribution of infants by birth week and birth weight

Both ears of 70 babies were evaluated (140 ears). A positive result was obtained from all infants with bilateral TEOAE test. All high-risk premature infants received a positive (passing) result from the automatic ABR test. The difference between the V wave latency and amplitude values obtained from the right and left ear at all frequency and intensity levels was evaluated regardless of the gender, high risk prematurity and healthy neonate. In the statistical evaluation of the cases, statistically significant differences were found in the latency values of high-risk premature and healthy newborns at all frequencies and intensity levels.

3. Mean, Standard Deviation, t and p Values of V Wave Latency Measurements Obtained by CE-Chirp Stimulus According to Right and Left Ear Stimulus Level for Newborn and Premature Participants at 500 Hz

According to the t-test results of the V. wave latency values obtained between the right and left ears at 500 Hz, a statistically significant relevance was found in 90 dB and 70 dB ($p<0.0001$), while

TABLE 1: Gender distribution of babies participating in the study.

Gender	High risk premature	Healthy newborn
Boy	19	16
Girl	16	19

TABLE 2: Distribution of infants by birth week and birth weight.

	High risk premature		Healthy newborn		
	Mean±Standard deviation	Median (Min-Max)	Mean±Standard deviation	Median (Min-Max)	p
Birth week	31.2±2.23	32 (26-34)	37.43±1.58	37 (35-41)	0.0001*
Birth weight	1701.71±569.1	1680 (730-3010)	2933.43±607.29	2880 (1710-4130)	0.0001*

there was a statistically significant difference between 50, 40 and 20 dB (p<0.05).

According to right and left ear measurements of V wave latency obtained in 500 Hz, the shortest latency was 4.40 ms at 90 dB and the longest latency at 9.24 ms at 20 dB.

4. Mean, Standard Deviation, t and p Values of V Wave Latency Measurements Obtained by CE-Chirp Stimulus According to Right and Left Ear Stimulus Level for Newborn and Premature Participants at 1000 Hz

According to the t-test results of the V. wave latency values obtained between the right and left ears at 1000 Hz, a statistically significant relevance was found in 90, 70, 50, 40 and 20 dB (p<0.0001).

According to right and left ear measurements of V wave latency obtained in 1000 Hz, the maximum latency was measured as 3.91 ms at 90 dB and 10.00 ms at 20 dB.

5. Mean, Standard Deviation, t and p Values of V Wave Latency Measurements Obtained by CE-Chirp Stimulus According to Right and Left Ear Stimulus Level for Newborn and Premature Participants at 2000 Hz

According to the t-test results of the V. wave latency values obtained between the right and left ears at 2000 Hz, a statistically significant relevance was found in 90, 70, 50, 40 and 20 dB (p<0.0001).

According to right and left ear measurements of V wave latency obtained in 2000 Hz, the shortest latency was measured as 3.73 ms at 90 dB, and the longest latency at 20 dB was 9.35 msec.

6. Mean, Standard Deviation, t and p Values of V Wave Latency Measurements Obtained by CE-Chirp Stimulus According to Right and Left Ear Stimulus Level for Newborn and Premature Participants at 4000 Hz

According to the t-test results of the V. wave latency values obtained between the right and left ears at 4000 Hz, a statistically significant relevance was found in 90, 70, 50, 40 and 20 dB (p<0.0001).

7. Mean, Standard Deviation, t and p Values of V Wave Amplitude Measurements Obtained by CE-Chirp Stimulus According to Right and Left Ear Stimulus Level for Newborn and Premature Participants at 500 Hz

According to the t-test results of the V. wave amplitude values obtained between the right and left ears at 500 Hz, a statistically significant difference was found in two ears of high-risk premature and healthy newborns at 90 dB and 20 dB in the left ears (p<0.05).

8. Mean, Standard Deviation, t and p Values of V Wave Amplitude Measurements Obtained by CE-Chirp Stimulus According to Right and Left Ear Stimulus Level for Newborn and Premature Participants at 1000 Hz

According to the t-test results of the V. wave amplitude values obtained between the right and left ears at 1000 Hz, a statistically significant difference was found in the right ears of 40 dB and 20 dB in two ears of high-risk premature and healthy newborns at 90 dB (p<0.05).

9. Mean, Standard Deviation, t and p Values of V Wave Amplitude Measurements Obtained by CE-Chirp Stimulus According to Right and Left Ear Stimulus Level for Newborn and Premature Participants at 2000 Hz

According to the t-test results of the V. wave amplitude values obtained between the right and left ears at 2000 Hz, a statistically significant difference was found in both ears of high risk premature and healthy newborns; 50 dB at left ears and 20 dB at both (p<0.05).

10. Mean, Standard Deviation, t and p Values of V Wave Amplitude Measurements Obtained by CE-Chirp Stimulus According to Right and Left Ear Stimulus Level for Newborn and Premature Participants at 4000 Hz

According to the t-test results of the V. wave amplitude values obtained between the right and left ears at 4000 Hz, a statistically significant difference was found in both ears of high risk premature and healthy newborns; 90 dB and 70 dB at left ears, 50 dB and 40 dB at right ears and 20 dB at both ($p<0.05$). In 70 dB, statistically significant difference was found in right ears.

DISCUSSION

The use of auditory evoked potentials is gradually increasing and becoming widespread. Auditory evoked potentials are an accurate and objective test measure, and can be very useful in evaluating children with speech disorders and in monitoring their therapeutic processes due to the patient's subjective response and the rapid plasticity of the nervous system.

The need to use multiple battery testing methods in clinical practice arises from the complex nature of the hearing system and the fact that hearing problems can be caused by pathology in one or more parts of this system. In addition, the use of multiple test batteries in audiological evaluation will prevent the possibility of being overlooked by the use of a single test. The clinician should complete the diagnostic tests with detailed history, observation and physical examination.[8]

The spread of current newborn screening programs requires the use of both otoacoustic emission and ABR. In 2007, "American Academy of Pediatrics Joint Committee on Infant Hearing" decided that each child under 6 months of age is required to perform frequency-specific ABR via bone and air. Also, it was decided to use tonal stimulus not only click stimulant during ABR.[7]

The most commonly used parameters in the diagnosis of ABR were I., III. and V wave latencies and I-III, III-V and I-V intermittent latencies. In the detection of threshold, the presence of V. wave is very important. I. and III. the waves do not always have detectable amplitudes in the intensity of stimulus near the threshold of hearing, however V wave can be seen even at the stimulus intensities very close to the hearing threshold. ABR wave latencies, inter-wave latencies and amplitudes may differ between clinics. CE-Chirp stimulus has been used recently to eliminate the problem with amplitude. An amplitude of at least two times greater than that of the conventional click stimulus is obtained.[6]

The type of stimulus and synchronized answers are important in threshold detection and clean records. To ensure this, electrical stimuli with short initial duration are required. The stimuli we use on the tonal audiogram are not enough to create this synchronized activity. Inadequate averaging in threshold determination is a major problem in ABR. The EEG amplitude may increase by 10 or even 100 times when the baby wakes up or moves.[9]

Elberling et al. showed that the use of ER-2 headphones for the click stimulus resulted in slightly larger amplitude waves than the ER-3A headphones, while the results for the chirp stimulus were slightly different.[10]

The use of ER-2 headphones in the chirp stimulus was much more effective than ER-3A, and ER-2 headphones with magnitude below 60 dB yielded significantly larger amplitude waves than ER-3A. This result has probably shown that the two headphones result from a large difference between the frequency-amplitude responses. In the studies, it was found that the amplitude responses of the ER-2 headset up to 1000 Hz were flat and the responses of 4000 Hz upstream of the ER-3A due to the bandpass filter were found to be decreased. The maximum difference between the two headphones was found to be approximately 35 dB at 8000 Hz.

The authors suggest that ER-2 headphones are preferable to ER-3A headphones in chirp stimuli in normal hearing adults at stimulus levels below 60 dB due to acoustic properties.[10] ER-3A (Etymotic Research) headphones are available in our clinic, and ER-3A headphones were used in our study for stimuli of all levels.

In the literature, 80 dB HL or lower stimuli were preferred as the upper limit in studies with CE-Chirp. In practice, testing is usually performed at 90-100 dB levels to evaluate auditory conditions in clinics. In our study, the tests were performed at 90, 70, 50, 40 and 20 dB HL levels.

Stutart and Cobb observed in a study on newborns that 464 repetition is required for CE-Chirp stimulus and 1856 repetition is required with click stimulus. Also, test time decreased significantly when CE-Chirp stimulus was used.[11] In another study of the same authors, test and re-tests were found to be reliable when CE-Chirp stimulus was used both by airway and bone.[12]

In a study, it was shown that when the stimulus rate was increased, the sensitivity perception increased, threshold sensitivity decreased but the threshold was not changed.[13] In clinical use, the preferred rate is 39.1/sec in adults and 11.1/sec in infants.

Rowe stated that the retro cochlear pathologies, which did not show any sign of low recurrence rate, became more prominent in the high repetition rate. It has been indicated that amplitudes have decreased in frequencies higher than 20 repetition rates.[14]

In our study, we adjusted the stimulus rate to 11.1/sec for all healthy neonates and high-risk prematures between the ages of 0-6 months.

It is known that sex has effects on ABR measurements. Latency increase in women and men is at different degrees. According to the literature, wave latencies in adult women are shorter than in men.[15,16] These differences in ABR wave and interwave latencies are tried to be explained by the shortness of neural pathways in women or by hormonal factors. In the literature, especially V wave latency has been shown to be significantly different between both gender.[17]

Stuart and Yang investigated the effect of gender on air and bone thresholds in newborns. When airway-induced stimulation was given, a shorter latency of 0.2-0.3 ms was observed in women. However, when the bone pathway stimulus is used, the latencies are equal.[18]

Cone Wesson and Ramirez argue that there is no effect of gender on the responses received with bone stimulus in newborns.[19] Ünlü, reported that there is no significant statistical difference between the absolute latency and inter-wave latencies in tb-ABR.

In our study, there was no statistically significant difference in V wave latency and amplitude values between the ages of 0-6 months in high-risk premature infants and healthy newborns.

In a study conducted by Jiank et al., the authors stated that the difference between the ears in 98% of the cases was less than 0.4 ms. The upper limit for the difference between the ears was reported to be 0.4 ms.[20]

Rosenhamer et al. showed that the difference between the ears and the gender effect, and found that the difference between the ears was less than 0.3 ms. They also reported that women had shorter latency values than men.[21]

While some researchers suggest that the cause of this difference is caused by the diameter of the head, the same results have been obtained from the studies of men and women with the same head diameter. It has been suggested that this finding may be due to the fact that women's hearing paths have shorter distances than men, differences in body temperature and hormonal levels.[22]

In our study, corrected age between 0 and 6 months of high-risk premature infants and healthy newborns were compared. According to this comparison, it was seen that the responses obtained from right ear in their groups had shorter latencies at the intensity of 90, 70, 50, 40, 20 dB at 500, 1000, 2000 and 4000 Hz and this was found statistically significant. When the amplitude values were compared between two groups, statistically significant differences were found in both ears at 90 dB at 500 Hz, in left ears 20 dB, in both ears at 90 dB at 1000 Hz, in right ears at 20 and 40 dB, in left ears at 50 dB at 2000 Hz, in both ears at 20 dB, in both ears at 20 dB, 70 dB, 90 dB at 4000 Hz, in right ears at 40 dB and 50 dB. There was no statistically significant difference between the right and left ears according to V. wave amplitude values.

In the literature, chirp stimulus was used in the studies and generally, V wave latency and amplitude were examined. When the studies taken into consideration, Increasing V. wave amplitude and shortening latencies reduce test duration according to click stimulus and provide threshold detection. However, since the majority of studies using chirp stimuli were performed in adults, more studies in premature and newborns will enable us to obtain more sound results on auditory neural maturation with V wave latency and amplitude values.

CONCLUSION

The ABR test is an electrophysiological method which can be measured audiologically and does not require patient involvement. Tests can be performed in infants, children, the elderly, unconscious or mentally retarded, as the patient does not require participation.

The grater amplitude of wave V is obtained at chirp stimulus than click stimulus that has the same frequency content, because travelling wave of chirp stimulus on the basilar membrane arrange according to the time distribution of frequencies.

The ability to obtain ABR waves with greater amplitude allows better quality and reliable ABR waves to be recorded at low intensity stimulus levels.

The use of adult ABR measurements for interpretation of ABR measurements in infants can lead to very serious errors in the diagnosis. For this reason, it is important to obtain reference values by determining normal ABR findings of infants.

In conclusion, considering that auditory neural maturation persisted up to 18 months, we obtained mean values that will help clinical interpretation of high-risk premature infants and newborns by using the V wave latency and amplitude values.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

***Idea/Concept:** Hatice Seyra Erbek, Veli Gencay Sungur; **Design:** Hatice Seyra Erbek; **Control/Supervision:** Hatice Seyra Erbek; **Data Collection and/or Processing:** Veli Gencay Sungur, Gülfem Beyazpınar; **Analysis and/or Interpretation:** Hatice Seyra Erbek, Veli Gencay Sungur, Gülfem Beyazpınar; **Literature Review:** Veli Gencay Sungur, Gülfem Beyazpınar; **Writing the Article:** Veli Gencay Sungur, Gülfem Beyazpınar; **Critical Review:** Hatice Seyra Erbek, **References and Fundings:** Veli Gencay Sungur, Gülfem Beyazpınar; **Materials:** Hatice Seyra Erbek.*

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