Comparison of cervical vestibular evoked myogenic potentials between late preterm and term infants

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SUMMARY: Ecevit A, Anuk-İnce D, Erbek S, Özkiraz S, Kurt A, Erbek SS, Tarcan A. Comparison of cervical vestibular evoked myogenic potentials between late preterm and term infants. Turk J Pediatr 2012; 54: 509-514.

Recent investigations have shown that late preterm infants have increased risk for attention deficit hyperactivity disorder, neurosensory impairment, and emotional, behavior and learning problems. Vestibular evoked myogenic potential (VEMP) abnormality may partly contribute to these problems. Our aim was to measure VEMP in late preterm infants and to compare the findings between late preterm and term infants.

Seventeen late preterm infants (mean gestational age: 35.11 weeks ± 0.78) postnatal aged 8 weeks and 17 full-term (mean gestational age: 38.05 weeks ± 0.96) infants postnatal aged 4 weeks underwent cervical (c)VEMP test without sedation. Mean latencies of p13 were calculated in all study subjects. cVEMPs were elicited in all late preterm and term infants. Mean latencies of p13 in late preterm and term infants were 14.53 and 13.34 ms, respectively. Mean latencies of n23 were determined as 23.18 ms and 19.92 ms for late preterm and term infants, respectively. There were statistically significant differences between late preterm and term infants for latency of p13 ($p<0.001$) and latency of n23 ($p<0.000$). Abnormal VEMP results might be related to a delay in the maturation of the sacculocollic pathways in late preterm infants.

Key words: late preterm infants, term infants, vestibular evoked myogenic potential, balance.

Late preterm birth is defined when a baby is born between 34 and 36 6/7 weeks of gestation[1,2]. The morbidity and mortality rate for late preterm infants are higher than for full-term infants[3,4]. Late preterm newborns represent approximately 74% of all preterm births and about 8% of total births[1]. The rate of late preterm deliveries has increased by about 25% during the last two decades. Late preterm births may result in increased risk for respiratory distress, patent ductus arteriosus, feeding difficulties, hyperbilirubinemia, hypoglycemia, and temperature instability, as well as higher rates of rehospitalization[5-10]. They also have more subtle neurodevelopmental problems like inferior academic performance[11].

Even though it is well known that delayed treatment of hearing loss in children causes impaired language development, the effects of vestibular system impairments in children are poorly understood. Children with vestibular deficit are generally considered uncommon. There are many symptoms of vestibular dysfunction, such as abnormal movement patterns, difficulty moving in the dark, behavioral changes, and/or delays in performance of developmental activities[12]. Significant deficits in standing balance performance were found recently in children with attention deficit hyperactivity disorder[13].

Cervical vestibular evoked myogenic potential (cVEMP) testing is a good indicator of saccular and inferior vestibular nerve function in the clinical evaluations of children[14]. Vestibular evoked potentials recorded by surface electromyography (EMG) electrodes are now widely used to assess vestibular function. The diagnostic utility of the cVEMP has also

been examined for neurological disorders and neurology or otology practice[15]. cVEMP testing is an electrophysiologic measure that is quick, and objective electrodes are placed over tensed sternocleidomastoid (SCM) muscles, and the initial positive (inhibitory) myogenic potential (p13-n23) is recorded in response to air-conducted sound[16]. Kelsch et al.[17] investigated 30 normal-hearing children aged 3 to 11 years who completed VEMP testing, and they found a mean latency of 11.3 ms, which was significantly shorter than in adult studies. Young et al.[18] showed that the mean p13 latency was 13.3 ± 0.8 ms in newborn infants by day 5. In another study by Chen et al.[19], there was a great variation in the maturation of the sacculocollic reflex at birth. Erbek et al.[20] investigated VEMP responses in four-week-old term infants. Recently, the time of VEMP testing was found to be inversely correlated with peak p13 values in preterm infants[21].

Our aim in this study was to determine the VEMP parameters in late preterm infants and to compare these parameters between late preterm and term infants aged 8 weeks and 4 weeks old, respectively.

Material and Methods

A total of 34 newborn infants were classified into two groups according to gestational age. These infants were late preterm and term babies. Late preterm birth was defined when a baby was born between 34 and 36 6/7 weeks of gestation. Seventeen late preterm and 17 term newborns aged 8 weeks and 4 weeks old, respectively, were enrolled in this study. Babies with multiple congenital abnormalities, respiratory distress syndrome, asphyxia, toxoplasmosis, rubella, cytomegalovirus, herpes simplex virus, or other congenital diseases, ototoxic drug use, intracranial hemorrhage, convulsions, hyperbilirubinemia, sepsis, steroid use (pre or postnatal), or a family history of hereditary childhood sensorineural hearing loss were excluded.

Infants were assessed by tympanometry, transient evoked otoacoustic emissions (TEOAEs), and cVEMPs. The parents of each newborn gave written, informed consent, and the Başkent University Institutional Review Board approved the study protocol.

Tympanometry

Tympanometric analyses were performed using GSI TympanoStar version 2 middle ear analyzer. Tympanograms were obtained at 1000 Hz probe tone. Subjects with middle ear pressures ≤ -50 mm H_2O were excluded.

TEOAE

Tests were performed using a TEOAE screener device "ILO292plus" (Otodynamics Ltd., Hatfield, UK) at five frequencies (1, 1.5, 2, 3, and 4 kHz). Stimulus stability of ≥75% and stimulus amplitude of ≥75 dB sound pressure level (SPL) confirmed the test validity. Criteria for having TEOAEs were a reproducibility rate of response higher than 50%, an overall signal-to-noise ratio of 3 dB SPL or greater, and a signal-to-noise ratio of response of 3 dB SPL for at least two frequencies.

VEMP

Surface EMG activity of the SCM muscle was recorded using the Smart EP25 device (Intelligent Hearing Systems). All infants were awake and no sedation was used. The active electrode was placed on the upper half of the ipsilateral SCM muscle, the reference electrode was attached on the suprasternal notch, and the ground electrode on the forehead. Late preterm and term infants were kept in the supine position on their mothers' laps. To contract the SCM muscle, the parent rotated the newborn's head as far as possible to the opposite side of the stimulated ear. The contraction of the SCM was controlled visually by an audiologist. Electrode impedance was below 5 μohm. The amplifier gain was set to 100,000, and signals and bandpass were filtered 10 to 3000 Hz. Short-tone bursts (100 dB nHL, 500 Hz, each, with 1 ms raise–fall time and 5-ms plateau time) were delivered monaurally by insert earphones. The stimulation rate and the analysis time were 5 Hz and 60 ms, respectively. A total of 128 responses to stimuli were averaged. Measurements were repeated twice to check test wave reproducibility. The first positive and negative polarities of the waveforms with peaks were named p13 and n23, respectively.

Interaural amplitude difference ratio was measured in both groups. It was calculated by

dividing the inter-ear difference of right p13-left p13 inter-amplitude by the sum of the right ear p13-left ear p13 and multiplying by 100.

Statistical evaluation

sPSS for Windows SPSS software (Statistical Package for the Social Sciences, version 11.0, SSPS Inc., Chicago, IL, USA) was used for statistical evaluation. The results were compared by Student's t and Mann–Whitney U tests. A p value <0.05 was considered to be statistically significant.

Results

In our study, the mean gestational ages were 35.11± 0.78 weeks and 38.05 ±0.98 weeks in late preterm and term infants, respectively. Table I reveals the demographic parameters of infants.

Table I. Demographic Characteristics of Late Preterm and Term Infants

Infants	Gestational age (mean±SD) (week)	Birth weight (mean) (g)	Girl	Boy
Late preterm	35.11±0.78	2344.11	11/17	6/17
Term	38.05±0.96	3164.70	8/17	9/17

Table II. Vestibular Evoked Myogenic Potential Parameters and p Values of Late Preterm and Term Infants

	Late preterm infants	Term infants	p value
Latency of p13 (ms) (mean±SD)	14.53±2.30	13.34±1.13	0.009
Latency of n23 (ms) (mean±SD)	23.18±2.70	19.92±1.58	0.000

All the study subjects passed the audiologic evaluation including tympanometry and TEOAE.

Table II shows the mean values of the VEMP test parameters (p13 and n23), and p values of the late preterm and term infants. The response rates of VEMP in late preterm and term infants were obtained, and mean latencies of p13 intervals were 14.53 and 13.34 ms, respectively. There were statistically significant differences between late preterm and term infants for p13 latency values (p<0.001). Latencies of n23 were determined as 23.18 ms and 19.92 ms for late preterm and term infants, respectively. A statistically significant difference (p<0.001) between late preterm and term infants was also determined for latency of n23 (Table II). Figure 1 shows p13 latency periods according to gestational age in preterm and term groups. Figure 2 shows cVEMPs responses for late preterm and term infants, and p13 latency periods were significantly longer in the late preterm group. The interaural amplitude difference ratio was calculated, and there was no statistical difference between the two groups.

Discussion

In our study, we investigated the VEMP parameters in both late preterm and term infants and found that there were statistically significant differences between the two groups for latencies of p13 and n23. VEMP is a well-tolerated clinical test for understanding vestibular function in children and adults. In 1964, Bickford et al.[22] showed the evidence for a short latency response in posterior neck muscles in response to loud clicks that appeared to be mediated by activation of the vestibular apparatus. In 1992, Colebatch and Halmagyi[16] demonstrated a patient with a short latency response to loud clicks studied using a modified recording site (the SCM muscles). The studies about VEMP in term and preterm infants are very rare in the literature. For the first time, in

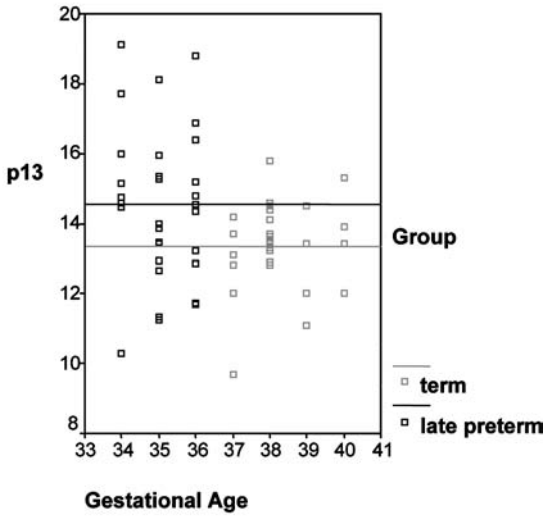

Fig. 1. Gestational age of infants and p13 latency values.

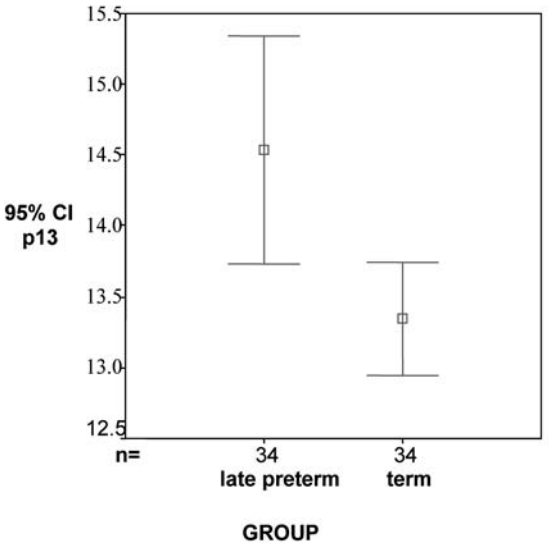

Fig. 2. VEMPs response (p13 values [ms]) for late preterm (34 ears) and term infants (34 ears)

2005, Sheykholeslami et al.[23] demonstrated that vestibular function in newborn infants could be noninvasively assessed using VEMP testing. In that study, 12 normal newborn infants and 12 neonates with various clinical findings were investigated. That study revealed a higher amplitude variability and shorter latency of the n23 peak in neonates when compared with adulthood waveform peak latencies. Otherwise, the overall measurement parameters of the neonatal VEMP were very similar to those of adults. Late preterm infants are at greater risk for short- and long-term complications. Respiratory distress, feeding difficulties, hyperbilirubinemia, hypoglycemia, temperature instability, higher rates of hospital readmission in the first month of life, and infection are common concerns for late preterm infants. Many studies found these problems, but few studies have shown that late preterm infants have increased risk of adverse developmental outcomes compared with term infants[11,24-28]. We thought that vestibular dysfunction can also cause motor and mental developmental delays in late preterm infants. Therefore, early recognition of health problems and early identification of vestibular dysfunction in late preterm infants are critical.

Young et al.[18] used VEMP parameters in newborn infants younger than two weeks of age. The majority of healthy full-term newborns demonstrated VEMPs by day 5, with a mean p13 latency of 13.3±0.8 ms during day 5. While significant prolonged p13 latency was found during day 3, no significant difference was observed between days 4 and 5. This test was found to evaluate the development and maturation of the sacculocollic reflex in newborns. The VEMP testing is a relatively noninvasive method. Erbek et al.[20] used VEMP test for early evaluation of vestibular dysfunction in healthy newborn infants. In that study, they investigated 24 term newborn infants with birth weight of more than 2500 g and Apgar scores higher than 7 at 1 minute. Mean latencies of p13, n23, and p13–n23 intervals were found as 13.7±1.1, 20.5±1.6, and 7.1±2.1 ms, respectively. That study showed that the fourth week was an appropriate time for measurement of VEMP testing in newborn infants. In our study, late preterm and term newborns were also enrolled at the ages of 8 weeks and 4 weeks, respectively. Chen et al.[19] also revealed that significant differences existed in the latency of p13, interpeak p13-n23 interval and p13-n23 amplitude between newborns and adults. They found the mean latency of n23 was similar to that of adults. VEMPs were investigated in preterm infants in another study[21]. Its aim was to determine the relationship between perinatal risk factors of prematurity and VEMPs. That study found no association between delayed VEMPs and gestational age, birth weight, hemoglobin and bilirubin levels, phototherapy, intracranial

hemorrhage, convulsions, sepsis, ototoxic drugs, transfusion, mechanical ventilation, retinopathy of prematurity, bronchopulmonary dysplasia, or respiratory distress syndrome in preterm infants. However, the most important risk factor for abnormal VEMP responses in preterm infants was asphyxia. There was also a significant difference in cVEMP testing between term and preterm infants in that study (29%; $p<0.001$)[21]. In our study, we compared the cVEMP parameters between late preterm and term infants and mean latencies of p13 were 14.53 and 13.34 ms, respectively. There was significantly delayed latency of p13 ($p<0.009$) and n23 ($p<0.000$) in late preterm infants. Hence, we found statistically significant cVEMPs differences in late preterm and term infant groups in our study. These findings might be due to immature myelination of the sacculocollic pathways in late preterm infants as well as preterm infants whose gestational ages were less than 34 weeks[19,21]. There are few studies on this issue in the literature, and also the full maturational process of vestibular function is not well known in premature infants. Sensory deficiency during early life produces lasting deficits in sensory functions[29]. Onset but not final maturation of vestibular function always occurs before birth[30]. Not only are the major milestones of vestibular morphological development occurring prenatally, the system begins functioning before birth as well[31]. In preterm infants, stimulation of gravistatic receptors is limited during the development of the vestibular organ. Reduced stimulation is correlated with decreased projections from the saccule to the medial vestibular nucleus and with reduced branching of gravistatic axons.

In conclusion, our study showed that term and late preterm infants had different VEMP parameters, and mean p13 and n23 latencies were prolonged in late preterm infants. The consequence of abnormal cVEMP responses may partly contribute to neurodevelopment disabilities in late preterm infants. Therefore, these infants should be followed closely for the vestibular deficiency-related complications.

Acknowledgement

This study was approved by Başkent University Institutional Review Board and Ethics Committee (Project no: KA06/120) and supported by Başkent University Research Fund.

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