The Evaluation of Visual Evoked Potentials (VEPs) Test in Premature Infants

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Abstract

Objective: Visual functions are under-developed in premature infants, as the visual pathways plexus beginning from optic nerves and extending to the visual cortex are affected in parallel with the incomplete myelinization process. Visual Evoked Potential (VEP) is a non-invasive and easily applicable method that provides information about the myelination process. The aim of this paper has been to analyze the evaluation of the VEP results in premature infants, the predictive value and its applicability in clinical practice.

Materials and Method:
Visual evoked potentials (VEPs) refer to the bioelectrical triphasic potentials initiated by flashing light stimulus and recorded by using amplifications and electrodes mounted on the head. It is electrographically based on the measurement of the formation period of the positive wave peak (P100 latency) in terms of milliseconds (ms). In the repeated measurements, as P100 latency gradually shorten; the maturation of visual myelization has been increased at that level. The VEPs tests were performed in our hospital within last 3 years, the premature infants were retrospectively analyzed.

Results:
A total of 197 [102 (51,8%) male, 95 (48,2%) female] premature infants including 75 very preterm, 54 moderately preterm, and 68 late preterm were included in this study. The mean latency (in milliseconds) of P100 wave was 138,94± 21,73; 140,40± 23,85 in the right and left eye respectively. P100 latency was found shorter in the right eye of late preterm as compared to extremely preterm (P:0,04), and in the left eye compared to very preterm and extremely preterm (P:0,02; P:0,03, respectively). P100 latencies of females were found to be shorter as from 18 months of (corrected) age (p: 0.02). In addition, it was seen that late preterm infants approached closer to normal values of P100 latency as compared to others (P> 0.05) after 12 - 18 months of (corrected) age.

Conclusion:
In our study, it was found that visual maturation was better in females; the most prominent maturation began in the period of 3-6 months of (corrected) age, it continued gradually in the following months, and visual maturation generally approached the final adult values by drawing a plateau between 12-18 months of (corrected) age.

Keywords: *Prematurity, VEP*

Introduction

The sense of sight is one of the most important feedback mechanisms for mental-motor development. This mechanism ensures the coordination of various organs (hand, body, feet, mouth, etc.) with the eye and enables learning related to many functions such as recognition and location of objects, sitting, walking, feeding, cognitive interaction, and behavioral profile. It achieves this by sending signals to vestibular and proprioceptive Systems (1,2).

Visual evoked potentials (VEPs) are one of the various parameters that provide objective evaluation of visual function (3,4). VEPs, by providing diagnostic information about the functional integrity of the visual system, help to gain insight into myelinization process of retinal development, cerebral development, synaptogenesis and nerve fibers (1,5,6).
Premature birth takes place before the development of the visual pathways of babies (3). Therefore, visual functions of premature infants are poorly developed since the myelinization process of visual pathways plexus extending from the optic nerves to the visual cortex is not yet complete as in other brain regions. VEPs test providing an idea about this process is non-invasive, cost-efficient and easy to apply method. In this study, it was aimed how VEPs results are evaluated in premature infants without major neurological disorders, the predictive value and its applicability in clinical practice.

Materials and Methods

Patients

The VEPs test performed in 197 premature infants including 75 very preterm, 54 moderately preterm, and 68 late preterm who were examined between 2016 and 2019 in Pediatric Neurology Department of Dr. Sami Ulus Beştepe Hospital was retrospectively analyzed; the data obtained were transferred to the electronic environment where statistical studies would be performed.
Visual Evoked Potentials (VEPs)
Despite the fact that many methods can be feasible in this test, flash-VEP technique is mostly used in infants and children, as the fixation ability of the eye is low (1,4). VEPs are bioelectrical triphasic potentials obtained by recording with the amplification system in a manner similar to electroencephalography (EEG) recording after active electrodes that collect neural signals for a given period of time following a flashing light stimulus given in the dark with the aid of a device (Nihon Kohden is used in our clinic) inserted to the occipital region (Oz, O1 ve O2), reference electrodes that collect non-neural signals to the frontal midline (Fz) and both ears' mastoid region, ground electrodes to the vertex (Cz). Numerous recordings made in this way are electronically averaged. Thus, while random EEG waves, in terms of temporal according to the externally applied signal are removed, evoked potentials (EP), which have temporal relationship to the stimulus, become apparent on the recording track. However, it should be attempted to ensure that the responses obtained by performing at least 2 consecutive averages are true bioelectrical potentials recorded and that it does not originate from any artifact sources. The temporal distance (latency or delay) of the obtained potentials to the stimulus and the amplitude of the subject potentials can be measured. It is electrographically based on the measurement of the formation period of the positive wave peak (P100 latency) in terms of milliseconds (ms) (Figure I) (4). In the repeated measurements, as P100 latency gradually shorten; the maturation of visual myelinization has been increased at that level (4,6).

Statistical Analysis

Data were analyzed via the SPSS 22.0 software; summarized in terms of mean±standard deviation and numbers (percent). X^2 test was used to compare the parameters with each other in terms of percentage as well as the descriptive statistics, t-test and the Mann–Whitney U test was used to compare mean where appropriate, and one-way ANOVA test for premature sub-groups. $P < 0.05$ was accepted as significant after the statistical analysis.

Results

A total of 197 [102 (51,8%) male, 95 (48,2%) female] premature infant including 75 very preterm [average age of gestation 28 weeks, 73±2,44 (23-31)], 54 moderately preterm [average age of gestation 32 weeks, 58±0,60 (32-33,8)], and 68 late preterm [average age of gestation 34

weeks, 75±1,20 (34-37)] were included in this study. The mean latency (in milliseconds) of P100 wave was 138,94± 21,73; 140,40± 23,85 in the right and left eye respectively (mean normal value in adults is approximately 102.3 ± 8). P100 latency was found shorter in right eye of the late preterm as compared to extremely preterm (P:0,04) and in the left eye as compared to very preterm and extremely preterm (P: 0,02; P: 0,03, respectively) (Table I). The latency of P100 waves was found significantly shorter (p:0,02) in females as compared to males after 18 months of (corrected) age (Table II). In addition, it was seen that late preterm infants approached closer to normal values of P100 latency as compared to others (P> 0.05) after 12 - 18 months of (corrected) age.

Discussion

In the study conducted by Kim et al., it is suggested that prolonged VEP latencies may be an indicator of psychomotor retardation (1). In other study, it was reported that VEP abnormality was found more common in premature infants as compared to full-term infants (7). In another study, it is emphasized that developmental delay may be present at the subclinical level in children with visual impairment even whose developmental stages are considered to be normal in the period from birth to 16 months of age (8). At this stage, VEPs test has become important in detecting low visual acuity at subclinical level.

VEP values have prognostic significance in asphyxiated newborns (9). Additionally, it was stated that it may give a clue about the neurodevelopmental process of cerebral palsy as early as 12 - 24 months (10-13). It was indicated that changes in P100 latency in the VEP test were significant in the first 6 months, it usually reaches the adult values around 1 year of age, and premature infants reach these values a little later (14-16). In our study, it was found that VEP P100 latency values were significantly shorter in late premature babies born after 34 weeks as compared to others (very preterm and moderately preterm). It was observed that VEP P100 latency values approached normal levels more especially on late preterm after 18 months of (corrected) age. In our study, it was also seen that females achieved normal values of P100 latency compared to males (p: 0.02) after 18th month of (corrected) age.

In a study similar to ours including 38 premature infants, it has been shown that there is an inverse correlation between VEP P100 latency and the magnitude of the gestational age and the postnatal age within the same gestational age, VEP P100 latency was found to be shorter among these (5). On the other side, in another study, there was no significant shortening of VEP P100 latency with age between premature infants and the control group (17). However, in this study, a rapid decrease in VEP P100 latency in the first 6 months, a gradual decrease between 6 and 12 months and a shortening between 12 and 18 months were reported to be continuous. As a result of this study, it was emphasized that VEP P100 latency was longer in infants with very low birth weight, and this length continues up to 18 months (corrected) age as compared to the control group. In our study, it was found that VEP P100 latency started to shorten in 3-6 months of (corrected) age period, especially in girls, it continued gradually in the following months, and visual maturation generally approached the final adult values by drawing a plateau between 12-18 months of (corrected) age (Figure II).

In conclusion, neurodevelopmental maturation correlates with myelization process in cerebral regions. There is no difference found between the visual pathways and other cerebral regions in terms of myelinization process. From another perspective, delays in myelinization of the visual pathways may give stimulating insight about the myelinization of other cerebral structures. Accordingly, in order to evaluate visual acuity as an indicator of myelinization, VEP test, which is an easily applicable, non-invasive and cost-effective method, should be evaluated. In this respect, VEP studies are one of the important steps in the evaluation of mental and motor developmental stages that are coordinated with vision in all childhood age groups beginning from infancy. Undoubtedly, abnormal VEPs results will shed light on the multidisciplinary

approach (neuro-ophthalmological examination, ergo-therapy, physical therapy, educational therapies) and will serve as a preliminary step towards more expensive tests such as neuroimaging, EEG.

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Table I: Demographic features and VEP P100 **latency**

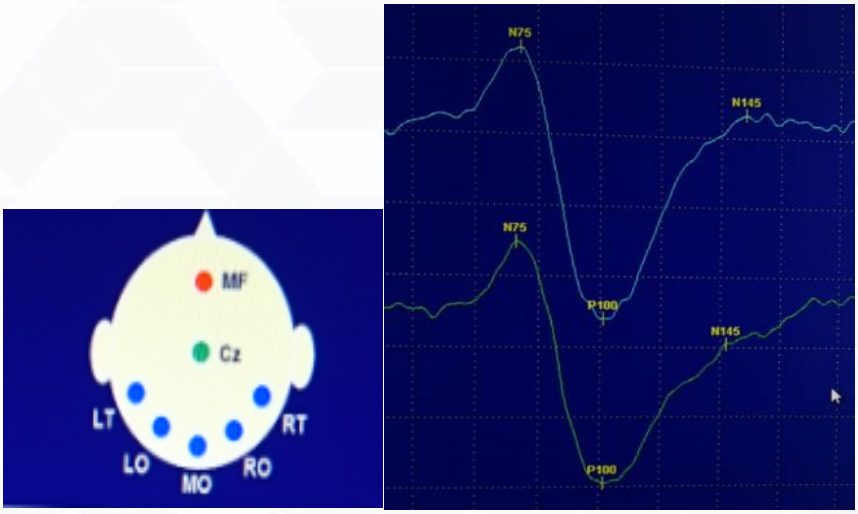
General features				
Gender(F/M) n_1(%)/n_2(%)	95 (48,2 %) / 102 (51,8 %)			
Birth week (mean±SD)	31,83±3,13			
Birth weight (gr; mean±SD)	1747±592			
VEP P100 latency (ms; mean±SD)	138,94±21,73 (Right eye) 140,40±23,85 (Left eye)			
VEP P100 latency distribution in Preterm subgroup(by ga)	n	%	Right eye (ms)	Left eye (ms)
Very preterm (< 32)	75	38,1	143,69±22,40	145,84±24,29
Moderately preterm (32-34)	54	27,4	140,99±21,08	143,06±23,2
Late preterm (34-36)	68	34,5	132,07±19,97	132,07±21,73
P value			0,04[a],	0,02[b], 0,03[c]

F: Female, M: Male, mean±SD: mean±standard deviation, gr: gram, VEP: Visual Evoked Potential,
ms: milliseconds, ga: gestational age,
a and b: significant correlation between late preterm and very preterm, c: between late preterm and moderately preterm

Table II: **Gender distribution in the >18 month of age VEP test**

VEP P100 latency	Right eye (ms)	Left eye (ms)
Female	104,32±1,99	105,37±2,97
Male	127,33±24,07	126,96±23,50
P value	0,02	0,02

VEP: Visual Evoked Potential, ms: milliseconds



A B

Figure I: VEP connection (A) and VEP bioelectrical potential of a patient (B)

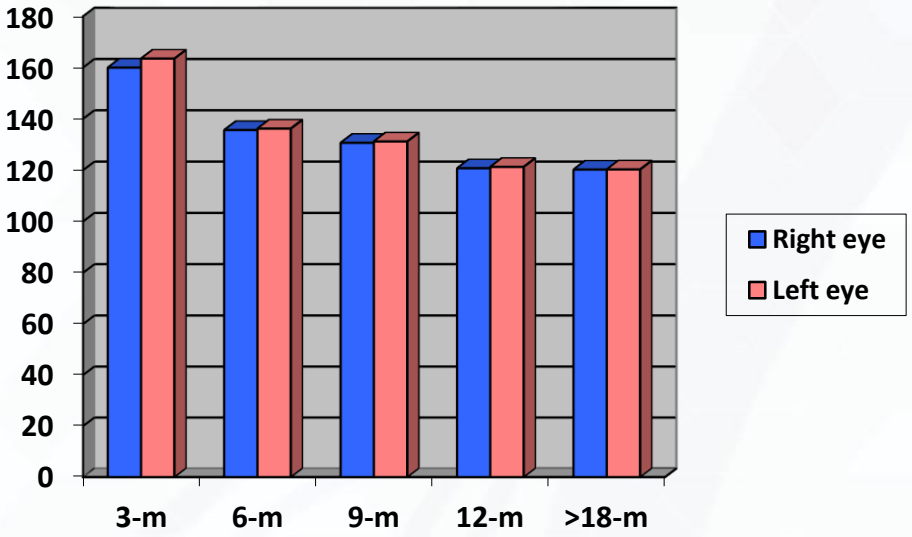


Figure II: VEP P100 latency according to corrected ages (in milliseconds), m:mounth