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Prolongation of interpeak latency of brainstem auditory evoked potential in hypothyroidism

***M. Jayanthi[1] and R. Vinodha[2]**

Department of Physiology, Thanjavur Medical College, Thanjavur

ABSTRACT

Hypothyroidism is a syndrome characterized by the clinical and biochemical manifestation of thyroid hormone deficiency. BAEPs are effective in evaluating the integrity of the peripheral and central auditory pathways. This study was undertaken to compare the interpeak latency of BAEP between hypothyroid patients and normal subjects. Forty patients [mean 39.7±12.5] with biochemical evidence of hypothyroidism, with thyroxine less than 4µg/dl and thyrotropin above 4.5 m IU/L including both gender were taken as a study group and compared with control group who were normal subjects and age and sex matched. Informed consent was obtained. Experimental protocol was approved by ethical committee. Both study and control groups were subjected to physical examination and laboratory investigations including triiodothyronine, thyroxine, and thyrotropin. BAEP recording was done by using four channel digital polygraph. The results were statistically analyzed using student't' test. P < 0.05 was accepted as significant.The result of present study shows significant prolongation of Interpeak latency of BAEP in study group compared to control group which suggest central nervous involvement in hypothyroidism.

Keywords: Hypothyroidism, Interpeak latency, Brainstem Auditory Evoked potential [BAEP], thyroxine, TSH

INTRODUCTION

Hypothyroidism is one of the most common endocrine disorders, affecting over one percent of the general population and about 5 percent of individuals over age of 60 years [1, 2]. It is a syndrome characterised by the clinical and biochemical manifestation of thyroid hormone deficiency in the target tissue [3]. Thyroid hormone regulates the timing and pace of development of the central nervous system [4]. They regulate neuronal proliferation, and differentiation, myelinogenesis, neuronal outgrowth, and synapse formation [5]. Thyroid hormone also enhances alertness, wakefulness, and learning capacity, auditory sense, and awareness of hunger, memory, and responsiveness to various stimuli. Furthermore, the speed and amplitude of peripheral nerve reflexes are increased by thyroid hormone [4]. The metabolic abnormalities, decreased cerebral blood flow or abnormal depositions of mucopolysaccharide that usually accompany hypothyroidism are believed to cause these symptoms [6]. These CNS manifestations are largely reversible with treatment [7].

Evoked potential recordings are useful in evaluating lesions in the afferent pathways under study. They assess the functional integrity of these pathways, whereas imaging techniques such as MRI and CT are useful in evaluating structural lesions of the brain. Thus, evoked potential studies sometimes reveal abnormalities missed by magnetic resonance imaging and vice versa. In patients with known CNS pathology, evoked potential studies help to detect and localize lesions and also detect structural abnormalities in a variety of disorders [8].

Brainstem auditory evoked potentials (BAEPs) are the potentials recorded from the ear and the scalp in response to a brief auditory stimulation to assess the conduction through the auditory pathway up to midbrain. The evoked potentials that appear following transduction of the acoustic stimulus by the ear cells create an electrical signal that is carried through the auditory pathway to the brain stem and from there to the cerebral cortex [9]. BAEPs comprise five or more waves within 10ms of the stimulus [10]. It may describe in terms of duration of onset of response [11].

BAEPs are useful to study in means of objectively and noninvasively the function of the auditory system, specifically the cochlea-auditory nerve-brainstem pathway, resulted in an extensive development of scalp recording of both near and far field potentials [12].

A. R. D. thornton and S. J. Jarvis showed a statistically significant reduction in the amplitudes of waves III and V and significant increase in the I-V interpeak latencies in hypothyroid patients. The measured abnormalities in I-V interpeak latencies may be explained on the basis of patients low body temperature [13].

Karlos Thiago Pinherio Dos Santo et al has done audiological evaluation in patient with acquired hypothyroidism and observed prolongation of absolute latency of wave I and the transient evoked otoacoustic emission were not present in a higher number of patients with hypothyroidism (20%) [14].

Yi-Hung Chou and Pen-Jung Wang was studied Auditory Brainstem evoked potentials in early treated congenital hypothyroidism and found prolongation of absolute latency of wave I, III, and V in hypothyroid patients [15].

Ritter showed that hearing loss can be the most common otorhinolaryngological manifestation of congenital and acquired hypothyroidism and auditory symptoms may happen alone or in association with vertigo and tinnitus [16]. Hence the electrophysiological study was done in hypothyroid patients, even in the asymptomatic ones, early in the course of disease in order to detect the nervous system involvement.

AIMS AND OBJECTIVES:

- This study was undertaken to compare interpeak latency of BAEP between hypothyroid patients and control.
- To evaluate functional changes in nervous system in hypothyroidism by Brainstem Auditory evoked potential.

MATERIALS AND METHODS

This study was conducted in the Department of Physiology, Thanjavur Medical College & hospital, Thanjavur. Case control type of study was done. The study period extended between may 2011 to Dec 2012. The patients were selected from medicine and surgery department.

Out of 40 patients, 7 males and 33 females with Hypothyroidism of age group (17-64 years) were selected. Out of 40 controls, 10 males, 30 females, of age group (17-64 years) were selected. Diagnosis of hypothyroidism was confirmed when the total thyroxine level was below 4µg/dl and the thyrotropin level was above 4.5mIU/L. A history was taken and a complete neurological examination was done. Subjects with Diabetes mellitus, Neurological disorders, Psychiatric illness, Seizures. Hypertension, Hearing abnormalities, ENT surgeries, vertigo, Eye diseases (severe myopia, cataract, glaucoma etc), Collagen disease, Drug abuse and Renal impairment were excluded.

The nature of study was explained to all the subjects. Informed written consent was obtained from all the participants. The experimental protocol was approved by the ethical committee. The thyroid profile was carried out using ELISA method. BAEP was recorded using four channel digital polygraph. Digital intex colour monitor, 17''model no: IT-173 SB.

METHODS OF RECORDING OF BAEP:

Electrodes are positioned using 10-20 electrode placement system [17].

PRETEST INSTRUCTIONS:

1. The subject was told about the procedure of the test and got informed consent.
2. The subject is asked to avoid applying hair spray or oil after the last hair wash.
3. Examination of external ear, Rinne's test, and Weber's test are carried out.
4. Subject is made to fully relax.
5. Mild hypnotics can be used to ensure relaxation.
6. Room should be quite and comfortable.

INSTRUMENT SETTING FOR BAEP:

Settings	BAEP
Sweep	5msec
Sensitivity	10µv
Low cut	100Hz
High cut	10Hz
pulse	11/sec
Pulse width	0.1 msec
notch	On
Decibels	60Db
Recordings	100 average was recorded using Click sound as stimulus.

PROCEDURE:

1. The skin is prepared by abrading and degreasing.
2. The electrode placement is at

Channel 1 =Cz-Ai (ipsilateral ear)
Channel 2= Cz-Ac (contra lateral ear).
Ground electrode is placed at 20%from the nasion Fz.

3. Head phones are placed on the ears for delivery of the auditory stimulus.

Clicks are delivered at the rate of 8-10/sec. Intensity to set at 60 db.
About 100 average is taken.

4. From the waveform obtained wave I and V is marked first.

Wave I is the first major up going peak usually follow a small stimulus artefact.

5. Wave V appears at approx 6ms and is often combined with wave IV in to a single complex waveform. Wave III is the major peak between wave I and V .Wave II is typically the first major upward deflection in the Cz –Az waveform as wave I is markedly attenuated or absent there.
6. From the above waveform inter peak latency I-III, III-V and I-V is obtained.

RESULTS

Out of 80 subjects, 40 were hypothyroid patients forming the study group and remaining 40 were normal subjects forming control group.

In this study, mean age for hypothyroid patients who form the study group was 39.7 ± 12.5 and the control groups was 35.8 ± 12.5. The mean values and standard deviation of thyroid hormone levels & Inter peak latency of BAEP for the control group and the study group were tabulated. Inter peak latency of BAEP was prolonged in study group compared to control group and the differences was statistically significant.

'P'value was derived from data analysis by using statistical package SPSS version 18 and statistical analysis was done by student't' test. The statistical significance was considered at p value < 0.05.

Table 1: shows that there is a significant difference between control group and hypothyroid group in T_3, T_4, TSH levels

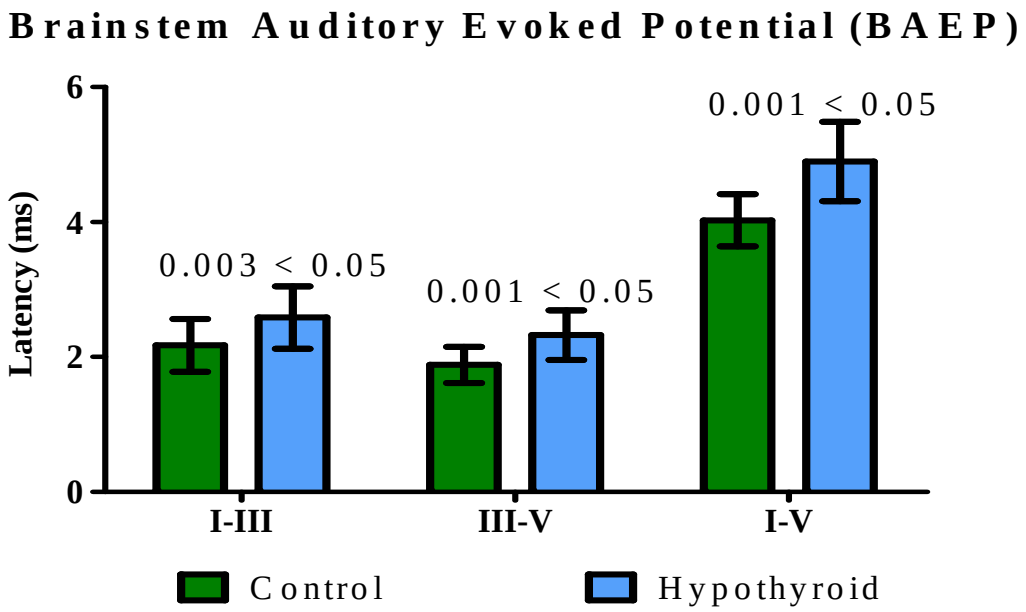
Parameters	Hypothyroid [n=40]	Control [n=40]	P value
	Mean ± SD	Mean ± SD	
Triiodothyronine[T3] [ng/dl]	0.3867±0.37450	1.1458±0.88295	0.001
Thyroxine[T4] [µg/dl]	2.3900 ± 0.74477	9.0480±3.98983	0.001
Thyrotropin [TSH] [mIU/L]	9.5910 ±5.30216	2.0575±0.95195	0.001

Triiodothyronine, Thyroxine, thyrotropin levels of hypothyroid patient are statistically significant with a P value of 0.001 respectively compared with control.

Table 2: shows that there is a significant difference between control and hypothyroid group in Interpeak latency of BAEP

BAEP Inter peak latency	Hypothyroid [n=40] Mean ± SD	Control [n=40] Mean ± SD	P value
Right ear			
I-III	2.6225±.60412	2.1367±.47451	0.001
III-IV	2.3340±.54091	1.8917±.40594	0.001
I-V	4.9565±.64327	3.9830 ±.46628	0.001
Left ear			
I-III	2.5440±.49215	2.2072 ± .48171	0.003
III-IV	2.3155±.45581	1.8705±.39488	0.001
I-V	4.8330±.64431	4.0675±.45641	0.001

Figure 1: Comparison of BAEP I-III, III-V, I-V interpeak latency between control group and hypothyroid patients



DISCUSSION

In this study, the electrophysiological parameters are evaluated in patients with hypothyroidism. The results of the electrophysiological study were compared between 40 patients with hypothyroidism and 40 healthy euthyroid subjects.

Hypothyroidism, particularly when subclinical, is the most common endocrinological disorders, with a prevalence ranging from 4 to 10% of the adult population. Hypothyroid states have a multiple effects on structure, perfusion, and function of the CNS [18].

Central nervous system dysfunction is an important consequence of thyroid hormone deficiency. Although the peripheral nervous system has been extensively studied in hypothyroid patients by a variety of techniques, quantitation of the central nervous system derangements has been less precise. However clinical observations and a wide range of neuro imaging, electrophysiological and neuropathologic investigations conducted in recent decades have confirmed a deleterious effect of hypothyroidism on the morphological and functions of the CNS. In a recent study, PET and SPECT measurement of cerebral blood flow in hypothyroidism was associated with global, diffuse hypoperfusion[18].

However, early involvement of the CNS, unlike the symptoms of peripheral neuropathy is usually subclinical and can be detected only through neurophysiological investigations. Measurements of stimulus conduction within the CNS by means of evoked potentials allow sensitive and reliable detection of subclinical changes.

In this study, prolongation in the Interpeak latency of Brain Stem Auditory Evoked Potentials (BAEP) I-III, III-V and I-V was found in patients with hypothyroidism and was statistically significant.

Hearing is one of the most sensitive functions controlled by thyroid hormone, and early onset hypothyroidism (or) iodine deficiencies is known causes of deafness in humans and rodent model species. The thyroid hormone is required for the timely co- ordination of the complex set of differentiation events in maturing cochlea. Several studies[13-16] show prolongation of latency and inter peak latency of BAEPs.

Metin Ozata et al showed that low body temperature, diminished myelin production and alteration in cerebral metabolism during acute hypothyroidism may be the possible explanations for the prolongation of wave I latency of BAEP[19].

Ritter in his study showed that the symptoms relating to auditory pathway in hypothyroidism may be due to hyper osteosis of the otic capsule or central nervous system damage [16].

The latency depends on an intact, myelinated nerve as myelin and saltatory conduction are essential for fast action potential propagation in normal subjects. Slowing of conduction velocity or propagation of latency usually implies defect in myelination. The prolongation of BAEP I-III, III-V, I-V interpeak latencies were more significant and suggests central nervous system involvement.

The present study results signify that there is a definite neurological deficit in thyroid deficiency, which can involve the central nervous system at much earlier stage.

In hypothyroidism mentation is slow and cerebrospinal fluid protein is elevated. They affect mitochondrial oxidative activity, synthesis, degradation of proteins and sensitivity of tissue to catecholamines and hence demyelination occurs due to oxidative damage to myelin membrane and oligodendroglial cells. Thus the present study results from BAEP data indicated hypothyroidism affect myelination.

Peripheral and central nervous system alterations in hypothyroidism have shown that CNS is more vulnerable to the effects of hypothyroidism than peripheral nervous system. Therefore electrophysiological studies were suggested to be performed in hypothyroid subjects early in course of thyroid deficiency in order to detect nervous system involvement.

CONCLUSION

The result of present study shows that there is involvement of Central Nervous System in hypothyroidism. The hypothyroid patients showed prolongation of latency in electrophysiological studies.

This study suggests that periodic evaluation of hypothyroid patients to electrophysiological test will help in monitoring the progress of neuropathy and earlier detection of nervous system involvement to reduce the morbidity of hypothyroid patients.

However further studies are required to evaluate the correlation between the electrophysiological parameters and duration of disease so that preventive measures can be suggested to prevent the central nervous system involvement.

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