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RESEARCH ARTICLE

PROLONGATION OF VEP P100 LATENCY IN HYPOTHYROIDISM

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ABSTRACT

Hypothyroidism is a syndrome characterized by the clinical and biochemical manifestation of thyroid hormone deficiency. The present study was undertaken to examine the functional integrity of visual pathway. Visual evoked potential is a non invasive tool to assess the integrity of visual pathway. Forty patients (17- 64yearsold, mean 37.7) 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. VEP 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. P 100 latency of VEP was prolonged in study group compared to control group and the differences was statistically significant. The result of present study shows significant prolongation of P100 latency of VEP suggestive of central nervous involvement in hypothyroidism.

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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 (Eugene J. Barrett, 2009, Paul A FitzGerald, 2012) Thyroid hormones are essential for early brain development and play a key role in later brain function (Joanne F Rovet, 2009) Thyroid hormone deficiency is associated with peripheral and central nervous system dysfunction. The Central nervous system manifestations include slowing of all intellectual functions, lethargy, somnolence, loss of initiative, memory defects, depression and rarely convulsions and coma (Anjana *et al.,* 2008). The metabolic abnormalities decreased cerebral blood flow or abnormal depositions of mucopolysaccharride that usually accompany hypothyroidism are believed to cause these symptoms (Eman M. Khedr *et al*., 2000). These CNS manifestations are largely reversible with treatment (Steven C. Boyages, 2000). Involvement of central nervous system in overt hypothyroidism has previously been shown by (Mastaglia *et al*., 1978, Avramides *et al.,* 1992, Eman Kedhr *et al.,* 2000) on the basis of visual evoked potential in adult. Ladenson *et al.,* 1984 conducted a study of visual evoked potentials in hypothyroid patients and found prolongation of P100 latency ($P<0.05$) following 12 to 24 weeks of long term oral L-thyroxine treatment. The mean P100 latency was significantly reduced ($P<0.001$) and it was concluded that reversible alteration of this readily measurable parameter in hypothyroid patients reflects an effect of thyroid hormones on central nervous system function. Salvi *et al.,* 1997 studied VEP in patients with TAO (thyroid associated ophthalmopathy) and observed prolongation of P100 latency in hypothyroid patient and showed that patient with TAO reveals asymptomatic optic nerve dysfunction in the absence of deterioration of visual acuity.

Evoked potentials are voltage changes monitored from the electrically excitable tissue if the cerebral cortex, brainstem, and spinal cord in response to various applied sensory stimuli. The function of pathways leading to three different central nervous system sensory areas, the Somatosensory cortex, the visual cortex, and the auditory region of the brainstem, can be evaluated using electro physiologic test (Andrew J. Robinson, 2008). Evoked potentials are particularly suited for a non invasive evaluation of a number of afferent pathways in the nervous system (Coot J. Bongers-Schokking *et al.,* 1991). Evoked potentials are frequently used to evaluate central nervous system physiology (Ronald G. Emerson, 2005). 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.

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Thus, evoked potential studies sometimes reveal abnormalities missed by magnetic resonance imaging and vice versa. In patients with known CNS pathology, evoked potentials studies help to detect and localize lesions and also detect structural abnormalities in a variety of disorders (Michael J. Aminoff, 2007). 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.

Aim and Objectives

- This study was undertaken to compare VEP P100 latency between hypothyroid patients and control.
- To evaluate functional changes in nervous system in hypothyroidism by visual 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 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, 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. Pattern reversal VEP was recorded using four channel digital polygraph. Digital intex colour monitor, 17''model no: IT-173 SB.

Method of Recording VEP

Electrodes are positioned using 10-20 electrode placement system (Jain, 2009)

Pre test instructions

- The subject was told about the procedure of the test and got informed consent.
- The subject is asked to avoid applying hair spray or oil after the last hair wash.
- If the subject uses optical lenses, glasses should be worn during the test.
- The subject is instructed not to use any miotics and mydriatics 12 hours before the test.
- Full ophthalmological examination was carried out to determine visual acuity, pupillary diameter and field of vision.
- The room should be quite and comfortable.

Recording of VEP: Instrument setting for VEP

Setting	VEP
Sweep	20msec
Sensitivity	10µv
Low cut	2Hz
High cut	200Hz
Pulse	1/sec
Pulse width	0.1msec
notch	Off
Recordings	100 average was recorded using Checker board pattern stimulus given

Procedure

The pattern-shift visual evoked potential was measured separately for each eye by following steps.

- The skin is prepared by abrading and degreasing.
- The recording electrode is placed at O_Z using electrode paste as per 10-20 international system of EEG electrode placement.
- The reference is placed at FPz.
- The ground is placed at the vertex (i.e.) at Cz
- The procedure is conducted in dark room with subject sitting at a distance of a 1 meter from the VEP screen showing pattern reversal stimuli in check board pattern with reversal rate 2/sec, contrast 50-80%, check size 28-32 of arc and number of trails is 100.
- From the waveform obtained (Figure 1) P100 latency is marked. P 100 is a positive potential at about 100ms.

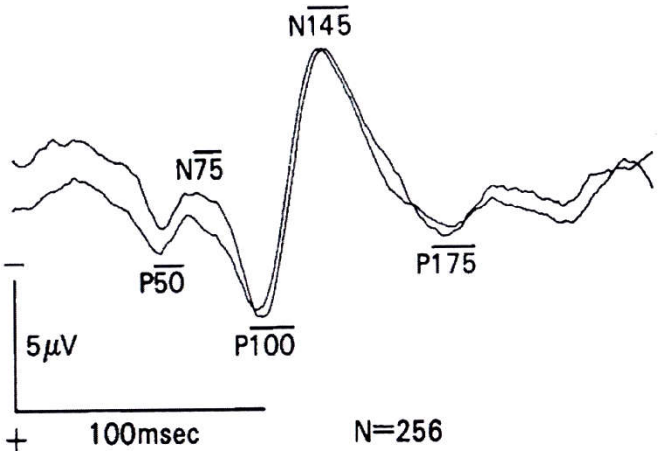

Figure 1. VEP showing P100 Latency

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 hypothyroid patients who form the study group were in age group 17-64 years, mean 39.64 and the subjects in control groups were in the age group 17-64 years, mean 35.75.

The mean values and their standard deviation for the control group and the study group of hypothyroids were tabulated. P 100 latency of VEP 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 controls.

Table 2. shows that there is a significant difference between control and hypothyroid group in latency P100 VEP

VEP P100 Latency	Hypothyroid (n=40)	Control (n=40)	P value
	Mean ± SD	Mean ± SD	
Right eye	103.66 ± 5.65	95.69 ± 4.10	0.001
Left eye	102.58±5.30	96.13±3.98	0.001

VEP P100 latency of hypothyroid patients was statistically significant with a P value of 0.001compared with controls.

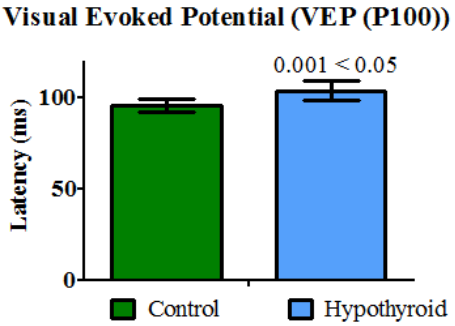

Figure 2. Comparison of VEP P100 latency between control group and hypothyroid patients

DISCUSSION

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, Visual evoked potential was evaluated in patients with hypothyroidism. The result of the visual evoked potential was 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 (Maximilian Pilhatsch *et al.,* 2011). 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 (Ladenson *et al.*, 1984). 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 (Maximilian Pilhatsch *et al.,* 2011). In this study, P100 latency of VEP is prolonged in patients with hypothyroidism and was found to be statistically significant.

This study results are consistent with those of Khedr *et al.*, Mastalgia *et al.*, Ladenson *et al.*, Salvi *et al.*, Avramides *et al.*, Ladenson *et al.* showed significant prolongation of P100 latency of VEP in hypothyroid patients, and reported that P100 latency of VEP was returned to normal on treatment with L-thyroxin and suggested that thyroid hormones have been shown to affect myelin synthesis, which is an important factor in determining the speed of impulse transmission along complex polysynaptic pathways such as those mediating the visual evoked potential. The reversible alteration of this readily measurable parameter in the hypothyroid patients reflects an effect of thyroid hormones on Central Nervous System.

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 cortical wave latency P100 suggests there is 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 VEP 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. Electrophysiological parameter like P100 latency of VEP was

evaluated. The observation shows prolongation of P100 latency suggestive of central nervous system involvement in hypothyroidism. 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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