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Original Research Article

Visual evoked potentials' responses in hypothyroidism and hyperthyroidism

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ABSTRACT

Background: Visual Evoked Potentials (VEP) provides important diagnostic and prognostic information regarding the functional integrity of the visual system. This study, describes the effects of less or excess thyroid hormones of adults in visual conduction that helps to know the progression to neurological functional defects.
Methods: The study was done in 75 consenting subjects (hypothyroid = 24, hyperthyroid = 25, euthyroid = 26). The VEP parameters N75, P100, N145 latencies and its amplitudes within different thyroid status (hypothyroidism, hyperthyroidism and euthyroidism) were compared. One way ANOVA was used to compare VEP parameters among three groups and Pearson's correlation to find relation between thyroid hormones and VEP parameters.
Results: There was positive correlation of 0.335, 0.338 and 0.301 between amplitudes of N75, P100 and N145 waves and fT_3 hormone respectively. Furthermore, fT_4 showed a positive correlation of 0.186 and 0.185 with the wave amplitudes of N75 and N145 waves respectively and negative correlation of TSH levels of -0.492, -0.280, -0.397 with amplitudes of N75, P100, N145 waves respectively. Hyperthyroid group had higher in VEP latency than euthyroid group in N75 (73±5.77 vs. 68.54±4.32), P100 (106.42±9.74 vs. 100.94±8.17) and N145 (153.03±16.39 vs. 144.37±7.02) waves. Similarly, hypothyroid group had higher in VEP latency than euthyroid group in N75 (72.12±6.34 vs. 68.54±4.32) wave.
Conclusions: Both hypothyroidism and hyperthyroidism led to conduction delay in adults, possibly adversely affecting function of myelin. The prominent visual evoked potential abnormalities in hyperthyroidism and less change in hypothyroidism show that the visual neuropathy is more common in hyperthyroidism.

Keywords: Hyperthyroidism, Hypothyroidism, Optic neuropathy, Visual evoked potential

INTRODUCTION

Thyroid hormone exerts effects on the brain throughout development, but the specific effects are different as development proceed.[1] The hypo or hyper secretion of thyroid hormone affects profoundly in fetal and neonatal brain but there is a poor documentation for its effects on adults' visual pathways.[2,3] Visual Evoked potentials (VEP) measure the time that it takes for a visual stimulus to travel from eye to occipital cortex. VEP has been used

extensively in the study of brain disturbances, optic atrophies, demyelinating diseases, compressive lesions affecting the visual pathway and to a lesser degree in metabolic diseases.[4] These effects are attributed to the loss or impairment in conduction of axons within the visual pathway.[5]

Visual Evoked Potentials (VEP) provide important diagnostic and prognostic information regarding the functional integrity of the visual system and this study describes the effects of less or excess thyroid hormones of adults in visual conduction that helps to know the progression to neurological functional defects affecting visual transmission, affecting the quality of life.

METHODS

The study was conducted in Neurophysiology lab in the Department of Basic and Clinical Physiology in collaboration with Department of Biochemistry, B. P. Koirala Institute of Health Sciences, Dharan.

It was a comparative multiple cross-sectional study and individuals were selected from a parent population using defined criteria and purposive sampling was applied.

The study was performed in both eyes of 75 subjects that included 24 hypothyroid, 25 hyperthyroid patients and 26 euthyroid healthy controls. The subjects meeting the exclusion and inclusion criteria were selected. Their anthropometric, cardiovascular parameters, serum fT_3, fT_4 and TSH were assessed. A detailed clinical examination of the subjects including neurological examination was done followed by electrophysiological recordings.

Inclusion criteria

All diagnosed hypothyroid and hyperthyroid patients as per their thyroid hormonal profile or thyroid function test (TFT) along with adult age group (18-45) were enrolled in the study.

Exclusion criteria

Age above 45 years, known neuropathy of any etiology, chronic smokers and alcoholic (for smokers the subjects with scores of Fagerstorm test for nicotine dependence ≥4 and alcohol use disorder identification (AUDIT) ≥8), any other along with disease of thyroid disorder or medicine that can affect VEP responses were excluded.

Measurements of hormonal profiles

Thyroid hormones viz. fT_3, fT_4 and TSH of the subjects were measured, based on combined a one-step enzyme immunoassay sandwich method with a final fluorescent detection.

Variables recorded

Anthropometric variables: age, height, weight and body mass index (BMI), Cardio-respiratory variables: heart rate, respiratory rate blood pressure and hormonal levels: fT_3, fT_4 and TSH were measured. Pattern reversal VEP (PR-VEP) waves N75, P100, N145 latency and their amplitudes amp N75, amp P100, amp N145 of both right left eyes were recorded consecutively.

Recording procedure for VEP variables

The recording procedure was started after fulfillment of above criteria for pattern reversal VEP. Equipment for measuring Pattern reversal VEP variables was Nihon Kohden machine (NM-420S; H636, Japan) provided with electrodes to record VEP waveforms and amplitudes.[6,7]

Electrode placement

The scalp electrodes were placed relative to bony landmarks, in proportion to the size of the head, according to the International 10-20 system. The anterior to posterior midline measurement was done based on the distance between the nasion and inion over the vertex. The electrode placement sites were cleaned with skinpure to reduce the skin resistance. Midline-occipital (MO) electrode, the active electrode, was placed 5 cm above the inion for single channel recording. We have preferred two channels recording i.e. CH-1 and CH-2 and montages used were right-occipital (RO)=5cm right of MO (midline-occipital) and left-occipital (LO)=5cm left of MO and midline-frontal (MF) i.e. the reference electrode, were placed 12cm above the nasion. Earthing electrode was placed on vertex (CZ). The electrodes were filled with Nihon Kohden Elefix gel, which acts as electrical conductor. Then electrodes were pressed firmly on the scalp.

Pattern reversal VEP (PR-VEP) recording

The subjects were instructed to sit on a chair in front of the T.V. monitor at a distance of 100cm from the screen to the eye. ONIDA14" color television (TV) displaying black and white pattern reversal checkerboard was used as visual stimulator. Small white squared fixation point in the center of the checkerboard was utilized for fixing the gaze and television was connected to the Nihon Kohden machine to record the waves of VEP. Patients were asked to fix their eyes on the central white fixation point (monocularly, i.e. one eye gently covered with hand). Checker size was 8˚ (stimulus field size). Visual field angle was 66 min of arc calculated by checker side length (38 mm). Filter was provided creating window of 1-100 Hz. Thus, PR-VEP was recorded. Signal was averaged 200 times automatically by machine which minimizes the signal to noise ratio. Any artifacts received were automatically shown by monitor as rejection. Recordings with rejections more than 25 times were discarded and recording was repeated. The reversal rate for pattern was

set at 1Hz with analysis time of 300ms. The recording procedure was of approximately 45min duration. The record of the VEP for each eye was done by channel-1 (RO-MF) and channel-2 (LO-MF) designated as A_1, A_2 waves respectively. Recording was repeated where waves were designated as B_1, B_2 for channel-1 and channel-2 to check the reproducibility of waveform. Similar, repetition of recording was done for the other eye.[7] The study was reviewed and accepted by the Ethical Review Committee of the institute (BP Koirala Institute of Health Sciences, Dharan). Informed consent was taken from all the participants and the methods followed to measure the parameters were entirely non-invasive.

The data obtained were entered in MS-Excel and analysis was done using Statistical package for Social Sciences (SPSS-20.0). The data were normally distributed. To compare among the three groups, one way ANOVA (post hoc analysis by Bonferroni) was applied. The Pearsonian correlation coefficient was used to find the association between the various variables. The data were expressed as mean±SD and p value less than 0.05 was considered as statistically significant.

RESULTS

In the tables below, p = comparison among the three groups by ANOVA, p1= p value of post hoc analysis (Bonferroni test) between hypothyroid and hyperthyroid groups, p2= p value of post hoc analysis (Bonferroni test) between hyperthyroid and control groups, p3=p value of post hoc analysis (Bonferroni test) between hypothyroid and control group. Table 1 showed the number of subjects according to the sex in hypothyroid, hyperthyroid and euthyroid control group with their age and BMI expressed in mean±SD.

Table 1: General parameters during the study.

Variables		Groups		
		Hypothyroid	Hyperthyroid	Control
Sex	Male	11	15	18
	Female	13	10	8
Age (years)		31.46±4.19	31.52±4.13	27.19±2.61
BMI (kg/m^2)		25.69±3.16	19.68±2.30	22.46±2.50

Table 2 showed the level of free T3, free T4 and TSH hormones in hypothyroid, hyperthyroid and euthyroid control group expressed in mean±SD.

Table 3 showed the correlation of thyroid hormones with VEP parameters. There were positive correlation of 0.335, 0.338, and 0.301 between fT3 and amplitude of N75, P100 and N145 waves respectively. Furthermore, there were a positive correlation of 0.186 and 0.185 of fT4, with the wave amplitudes of N75 and N145 waves respectively and negative correlation of TSH levels of -0.492.-0.280, -0.397 with wave amplitudes of N75, P100, N145 waves respectively.

Table 2: Hormonal profiles during the study in the groups.

Variables	Groups		
	Hypothyroid	Hyperthyroid	Control
fT_3 pg/ml	0.55±0.32	11.01±3.17	2.55±0.96
fT_4 ng/dl	8.48±5.83	8.48±5.83	1.56±0.74
TSH mIU/ml	12.17±2.29	0.16±0.28	3.51±1.53

fT_3 = free tri-iodothyroxine, fT_4 = tetra-iodothyroxine, TSH = thyroid Stimulating Hormone

Table 3: Pearson correlation of thyroid hormones with VEP parameters.

Variables		N75 ms	P100 ms	N145 ms	amp N75 µV	amp P100 µV	amp N145 µV
fT_3	"r"	0.123	0.127	0.166	0.355	0.338	0.301
	p value	NS	NS	NS	<0.001	<0.001	0.001
fT_4	"r"	0.129	0.136	0.013	0.186	0.117	0.195
	p value	NS	NS	NS	0.045	NS	0.036
TSH	"r"	-0.052	-0.095	-0.121	-0.492	-0.28	-0.397
	p value	NS	NS	NS	<0.001	0.002	<0.001

fT_3 = free tri-iodothyroxine, fT_4 = tetra-iodothyroxine, TSH = thyroid Stimulating Hormone, N75 = Latency of N75 waves, P100 = latency of P100 waves, N145 = latency of N145 waves, amp = amplitude, p1= p value of post hoc analysis (Bonferroni test) between hypothyroid and hyperthyroid groups, p2= p value of post hoc analysis (Bonferroni test) between hyperthyroid and control groups, p3=p value of post hoc analysis (Bonferroni test) between hypothyroid and control group

Table 4 showed the comparison of VEP variables among the three group i.e. hypothyroid, hyperthyroid and euthyroid control group. There were significant findings in the latency of N75, P100 and N145 waves and amplitudes of VEP. The latency of waves N75, P100 and N145 were higher in hyperthyroid and wave N75 was higher in hypothyroid group when compared with euthyroid controls. The delay in visual conduction was more in hyperthyroid group compared to hypothyroid group. Hypothyroid group had shorter amplitude of waves N75, P100, N145 than euthyroid group.

The prominent visual evoked potential abnormalities in hyperthyroidism and less change in hypothyroidism show that the visual neuropathy is observed more common in hyperthyroidism.

Table 4: Comparison of VEP variables (both eyes) among hypothyroid, hyperthyroid and control group.

Variables	Groups (Mean ±SD)			p value	Post hoc		
	Hypothyroid	Hyperthyroid	Control	p	p1	p2	p3
N 75 ms	72.12±6.34	73.00±5.77	68.54±4.32	<0.001	NS	<0.001	0.004
P 100 ms	103.73±5.92	106.42±9.74	100.94±8.17	0.004	NS	0.003	NS
N 145 ms	147.79±10.33	153.03±16.39	144.37±7.02	<0.001	NS	0.001	NS
amp N 75 µV	0.48±0.50	1.28±0.73	1.23±.61	0.004	<0.001	NS	<0.001
amp P100 µV	2.88±1.27	3.94±1.72	4.21±1.22	<0.001	0.001	NS	<0.001
amp N145 µV	0.58±0.87	1.86±1.37	2.15±1.48	<0.001	<0.001	NS	<0.001

N75 = Latency of N75 waves, P100 = latency of P100 waves, N145 = latency of N145 waves, amp = amplitude, p1= p value of post hoc analysis (Bonferroni test) between hypothyroid and hyperthyroid groups, p2= p value of post hoc analysis (Bonferroni test) between hyperthyroid and control groups, p3=p value of post hoc analysis (Bonferroni test) between hypothyroid and control group

DISCUSSION

Thyroid hormone appears to play a critical role in the development of the neuroretina particularly on how the hormone and its receptor isoforms influence retinal cell proliferation and cell fate decisions in developmental stage in fetal life and the alterations in thyroid hormone status is also said to modulate adult hippocampal neurogenesis.[1, 8] Thyroid disorders can either cause optic neuropathy or can be a risk factor for glaucoma.[9] Visual evoked potentials are a good way to assess demyelinating effects on visual conduction probably in relation to metabolic and structural alterations.[7,10] VEP pattern stimulation has been a sensitive diagnostic indicator of optic nerve compression as well.[9,11]

In our study, comparing the different thyroid status, the N75, P100 and N145 waves were prominent in hyperthyroid group compared to hypothyroid group. The wave amplitudes were higher in hyperthyroid group whereas the hypothyroid group showed delayed amplitudes in comparison with control. This showed that the visual neuropathy was observed in both hypo and hyper thyroid groups but more affected in hyperthyroidism.

Findings show that hyperthyroidism has been reported to prolong the latency of pattern VEP, especially P100.[12] In the study done by Aparajita et al in hypothyroid patients, VEP latency N75, P100, N145 was found to be prolonged as compared to the controls both on the right as well as the left eye. Similarly, VEP amplitude on both right and left side was lower in the hypothyroid cases as compared to controls.[13] Other findings similar to our study in hypothyroid patients were done by Khedr et al, Avramides et al, Ladenson et al which showed significant prolongation of VEP wave latency in hypothyroid patients and hyperthyroid patients compared to the euthyroid controls.[4,14,15]

In contrast, the findings done by Mitchell et al, showed that hyperthyroid status had little effect on conduction in the visual pathways showing slight latencies and increased VEP amplitudes.[16] Also, Salvi et al found that euthyroid or hypothyroid patients were not affected by the results of the VEP test except in case for hyperthyroid patients where there was prolongation of P 100 wave latency.[17] Nazliel et al, claimed abnormal VEP variables in hypothyroid patients but in small group setting and they suggested the abnormalities in wave pattern of VEP to be associated with advance thyroid disease states and in cerebellar dysfunction as well.[18]

The thyroid hormone affects the visual pathways and might be its most predominantly effect in demyelination and lesserly in neuronal plasticity, in ionic equilibrium and metabolic changes during the disorders in the eye but the exact mechanism is yet to be explored extensively at molecular levels in human/animal models which the study can direct a way alongside. Further, longitudinal studies before and after thyroxine therapy can be done in larger populations in males and females so as to know the progression to optic neuropathy, degree of latencies and its reversible or irreversible effects either in infants or adult population.

CONCLUSION

Both hypo- and hyperthyroidism led to conduction delay in visual evoked potential in adults. The prominent abnormalities in hyperthyroidism and less change in hypothyroidism show that the visual neuropathy is more common in hyperthyroidism. These changes possibly affecting the function of myelin since, T_3 and T_4 are known to affect myelinization and synaptic transmission. This would help patients to be aware of demyelization affecting visibility and thus, the quality of life.

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Ethical approval: The study was approved by the Institutional Ethics Committee of the BP Koirala Institute of Health Sciences, Dharan, Nepal

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