Sensory Neuropathy in Hypothyroidism: A Case-Control Study

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ABSTRACT

Introduction: Hypothyroidism is a endocrine disorder which results in neurological dysfunction. It also affects brain, peripheral nerves and muscular system. The neurologic manifestations, which may be noted incidently, occur in conjunction with the systemic features of the disease. Peripheral neuropathy occurs early in hypothyroidism and its detection is necessary for early diagnosis and treatment. Study aimed to know the sensory nerve conduction in patients of Hypothyroidism and to compare sensory nerve conduction parameters in patients of Hypothyroidism with normal healthy individuals.

Material and Methods: A case-control study conducted in 200 subjects aged 18 years and above (100 cases, 100 controls). The study was done in clinical neurophysiology unit of a rural teaching hospital in central India. In all subjects, nerve conduction study was performed using RMS EMG EP-II available in department of Physiology. Electrophysiological parameters like Sensory Nerve Action Potential amplitude and conduction velocity were evaluated.

Results It was found that sensory nerve action potential amplitude and conduction velocity were significantly reduced in Median and Sural nerves in cases as compared to controls.

Conclusion. Nerve conduction study very effective test for early diagnosis of peripheral neuropathy in Hypothyroidism.

Keywords: Hypothyroidism, Sensory neuropathy, Nerve conduction study

INTRODUCTION

The thyroid hormone is a key regulator of cellular metabolism in the body. The thyroid hormones maintain the various metabolic functions by stimulating the oxygen consumption in most of the cells of our body and are also necessary for their normal growth and maturation. The thyroid gland though is not essential for life; its absence causes mental and physical growth retardation.[1] Hypothyroidism is caused by the low level of circulating thyroid hormones and raised TSH. It is estimated to affect 3.8–4.6 % of general population, with four times common in women.[2] The most common cause of hypothyroidism in India is Iodine deficiency.

General clinical features of hypothyroidism includes tiredness and weight gain without appreciable increase in caloric intake, decreased heat production, lower body temperature, intolerance to cold and decreased sweating, constipation, fatigue, somnolence and hoarseness of voice.[3]

Hypothyroidism is a endocrine disorder which results in neurological dysfunction. It also affects brain, peripheral nerves and muscular system. The neurologic manifestations, which may be noted incidently, occur in conjunction with the systemic features of the disease. The symptoms and signs of neurologic dysfunction may be the presenting feature in some patients and can contribute significantly to disability.[4]

In adults, the neurological manifestations of clinical hypothyroidism include decreased mental status, bradycardia, hypothermia, poor concentration and short-term memory, peripheral neuropathy, entrapment neuropathy and myxedema coma. In some patients with clinical hypothyroidism, the main and presenting manifestation may be the peripheral nerve dysfunction. In overt hypothyroidism, the frequency and severity of neuromuscular disease depends mostly upon the severity and duration of thyroid hormone deficiency.[5]

In hypothyroidism, metabolic alteration occurs due to hormonal imbalance which affects the Schwann cell and induces a segmental demyelination. It has been shown electrophysiologically and pathologically that there is primary axonal degeneration.[6]

The function and the ability of electrical conduction of the motor and sensory nerves, can be evaluated by nerve conduction study. With the steady improvement and the standardization of these methods, nerve conduction studies have become reliable tests in clinical settings.

Nerve conduction studies often can define whether the underlying pathophysiology is demyelination or axonal loss and they can differentiate between a primary demyelinating and a primary axonal neuropathy.[7]

This study was done to observe the effects of hypothyroidism on nerve conduction parameters and for the evaluation of the role of nerve conduction study for early diagnosis of peripheral neuropathy in patients of hypothyroidism.

MATERIAL AND METHODS

A case control study was done which was carried out in Mahatma Gandhi Institute of Medical Sciences, Sewagram. This study was done in the patients of hypothyroidism 18 years and above for a period of two years from August 2012 to July 2014. The study was done in 200 subjects including 100 cases and 100 control. Cases were referred from department of Medicine.

Detail history of the subjects was taken including general signs and symptoms related to hypothyroidism, alcohol intake, smoking and any drug history. We also enquired the subjects about their demographic and socio-economic variables. Blood pressure measurement and anthropometric parameters were recorded in all subjects and determination of Serum total T3, total T4 and TSH was done by chemiluminescense assay. Patients suffering from diabetes mellitus, liver and kidney disease and patients with hypothyroidism secondary to pituitary

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disease were excluded from the study.

RMS EMG EP - MARK II machine was used for nerve conduction study which is available in clinical neurophysiology unit, Department of Physiology, Mahatma Gandhi Institute of Medical sciences, Sewagram. Sensory nerve conduction study was done in all subjects which included the determination of sensory nerve action potential (SNAP) amplitude and conduction velocity of median, ulnar and sural nerves.

Sensory nerve conduction study (antidromic) involved stimulation of sensory nerves proximally and recording SNAPs with electrodes placed distally over the dermatomic distribution. Sensory nerve conduction velocity was calculated by dividing the distance between active electrode and cathode of stimulator by onset latency. Sensory nerve action potential amplitude was taken from peak to base. Ground electrode was placed between stimulating and recording electrodes.

Antidromic study was done using ring electrode. Ring electrode was placed on index finger for Median nerve on little finger for ulnar nerve and surface disc electrode was placed posterior to lateral malleolus of ankle of foot for sural nerve. In all cases cathode and anode were 3 cm apart. For upper and lower limbs, duration was 100 µs, sweep speed 2 ms/D and filter was between 20Hz to 3 KHz.

STATISTICAL ANALYSIS

Descriptive and inferential statistics using chi square test and z-test for difference between two means, was used for Statistical analysis. SPSS 17.0 software was used for analysis and $p<0.05$ was considered as level of significance ($p<0.05$).

RESULTS

There was no statistically significant difference between control and cases of hypothyroidism in age and other anthropometric and biological parameters like height, weight, BMI, systolic blood pressure, diastolic blood pressure and pulse rate (Table 1). There was statistically significant decrease in Serum T3, T4 level and statistically significant increase in Serum TSH levels in cases as compared to control subjects as shown in Table 2. Nerve conduction abnormalities were found in patients of hypothyroidism as compared to controls. The sensory nerve action potential amplitude and conduction velocity were significantly reduced in cases as compared to controls.

In lower limbs the Sural nerve SNAP amplitude and conduction velocity were reduced significantly as compared to controls. In upper limbs the Median nerve SNAP amplitude and conduction velocity were reduced significantly in cases as compared to controls while in Ulnar nerve the SNAP amplitude and conduction velocity were reduced but it was not significant (Table 3).

DISCUSSION

Thyroid hormone is also known to influence the synthesis is of protein and the production of enzyme and of myelin sheeth.[8,9] Myelin synthesis is an important factor in determining the speed of impulse transmission along the nerve length[8,10]

Disturbed myelin synthesis during acute hypothyroidism may be the cause for demyelinating peripheral neuropathy in hypothyroid patients. Hormonal and metabolic changes associated with hypothyroidism are responsible for the electrophysiological changes in the form of abnormal peripheral nerve conduction study which occurs early in the disease course. SNAP amplitudes and CV were significantly reduced in cases as compared to controls in bilateral Sural and Median nerves ($p<0.05$).

Variables	Control Group		Case Group		Difference	z-value	p-value
	Mean	SD	Mean	SD			
Age (yrs)	48.13	12.32	47.48	12.20	0.72±1.73	0.410	0.679 NS, p>0.05
Ht (cm)	163.11	6.92	162.64	4.11	0.46±0.81	0.567	0.571 NS,p>0.05
Wt(Kg)	63.96	6.56	65.30	6.13	1.25±0.89	1.390	0.166 NS,p>0.05
BMI	24.05	2.24	24.64	2.08	0.58±0.30	1.917	0.57 NS,p>0.05
SBP	119.69	9.61	120.09	8.65	0.39±1.29	0.306	0.760 NS,p>0.05
DBP	76.91	7.18	76.97	8.76	0.06±1.13	0.060	0.952 NS,p>0.05
PR	76.66	4.19	76.26	4.12	0.40±0.58	0.682	0.496 NS,p>0.05

Table-1: Demographic characteristics in hypothyroid cases and controls.

Laboratory Parameters	Control Group		Case Group		Difference	z-value	p-value
	Mean	SD	Mean	SD			
Serum $T_{3(ng/dl)}$	76.86	14.83	62.60	25.66	14.25±2.96	4.80	0.000 S,p<0.05
Serum $T_{4(\mu g/dl)}$	7.61	2.49	5.56	4.80	2.05±0.54	3.79	0.000 S,p<0.05
Serum TSH(µIU/ml)	2.76	2.01	28.66	30.43	25.90±3.04	8.49	0.000 S,p<0.05

Table-2: Comparison of laboratory parameter in both the groups

Variables	Control Group		Case Group		Difference	z-value	p-value
	Mean	SD	Mean	SD			
Median							
CV(m/s)	49.81	6.16	45.15	6.71	4.66±0.91	5.113	0.000 S, p<0.05
Amplitude(μV)	16.15	4.95	12.46	4.94	3.68±0.69	5.271	0.000 S, p<0.05
Ulnar							
CV(m/s)	52.54	8.67	51.85	7.93	0.69±1.18	0.586	0.559 NS, p>0.05
Amplitude(μV)	13.69	4.11	13.15	6.51	0.53±0.77	0.693	0.489 NS, p>0.05
Sural							
CV(m/s)	50.96	8.13	41.32	8.24	9.63±1.17	8.211	0.000 S, p<0.05
Amplitude(μV)	14.25	4.81	8.63	3.49	5.61±0.60	9.353	0.000 S, p<0.05

Table-3: Comparison of electrophysiological parameters in hypothyroid patients and controls (Sensory components right side)

Our Findings are supported by previous studies by Ettore Beghi et al (1989).[11] They assessed the prevalence and characteristic of polyneuropathy using standard clinical and electrophysiological tests in patients with primary hypothyroidism. They too have observed mild degree of sensory polyneuropathy in the patients. Marcia W.Cruz et al (1996)[12] reported sensory axonal polyneuropathy in 68.7% of patients with primary hypothyroidism. This observation is similar with our findings. Gülbün Yuksel et al (2007)[13] noted the similar findings of sensory polyneuropathy in subclinical hypothyroid patients.

Somay G et al (2007)[14] and Yeasmin S et al (2007)[15] electrophysiologically evaluated the patients of hypothyroidism and observed occurrence of sensory polyneuropathy in them especially affecting median and sural nerves. These reports coincide with our findings.

Nemni R Bottachi et al (1987)[6] proposed that degeneration of peripheral nerve in hypothyroidism is primarily axonal causing axonal polyneuropathy. Our findings are not co-existent with these findings as we observed mixed (axonal and demyelinating) type of lesion in the cases.

Thyroid hormone seems to increase ATPase activity and, consequently, the activity of the ATP-dependent Na+/K+ pump. The increase in ATPase activity would be associated with an increase of ATP transport through the mitochondrial membranes. In hypothyroidism, the ATP deficiency and the reduced activity of the ATPase enzyme induces a decrease in Na+/K+ pump activity, with consequent alterations of pump-dependent axonal transport. This leads to axonal degeneration and peripheral neuropathy in hypothyroidism.[6]

The mucinous infilterations found in the peripheral nerves could interfere mechanically with metabolic exchange of nutrients and catabolic products to and from the neuron resulting in entrapment neuropathy in hypothyroidism.[16]

The deposition of mucopolysaccharide or the myxomatous tissue around the peripheral nerves may also lead to its compression and thereby results in swelling and degeneration of those nerves leading to peripheral neuropathy in hypothyroidism.[17]

CONCLUSION

This study concluded that the polyneuropathy which is associated with hypothyroidism was largely of mixed type (axonal as well as demyelinating type). The detection of this abnormality suggests that nerve conduction study might be useful to evaluate and to diagnose peripheral neuropathy in hypothyroid patients.

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