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Peripheral Neuropathy in Hyperthyroidism - A Case Control Study

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ABSTRACT

Background: Thyroid hormone is the one that exhibits its effect on all the cells in our body. So any dysfunction of thyroid gland secretion either decreased or increased has its effects on all the systems in our body. There are many studies in hypothyroidism and nervous system and only few studies done in patients with hyperthyroidism as neuropathy is found to be uncommon in hyperthyroidism.
Aim: To perform Nerve Conduction Study in Hyperthyroid female subjects and age matched controls and compare the results.
Materials and Methods: This is a case control study conducted in Tirunelveli Medical College Hospital after getting IEC approval. The study was performed in 18 newly diagnosed hyperthyroid female patients and 25 control subjects. The mean age of Hyperthyroid patients is 34.72 $\pm$ 8.75 and control is 36.52 $\pm$ 8.10. The sensory nerve conduction study was performed in Sural, Median and Ulnar nerve. The motor nerve conduction study was performed in Posterior Tibial, Median and Ulnar nerve. The nerve conduction studies were done using RMS EMG EP MARK II at Neurophysiology lab.
Results: The nerve conduction study parameters like Latency, Conduction Velocity and Amplitude of motor and sensory nerve of Hyperthyroid and control subjects were compared and statistical analysis done by unpaired t test. There was a statistically significant difference between hyperthyroid and control subjects predominantly in sensory nerve conduction study. Sensory neuropathy was present in 61% and sensorimotor neuropathy in 5.5% and carpal tunnel syndrome in 17% of hyperthyroid subjects.
Conclusion: It is essential to include nerve conduction study as a routine in hyperthyroid patients also.

Keywords: Hyperthyroidism, Nerve conduction study, Amplitude, Latency, Conduction velocity

INTRODUCTION

Thyroid hormone is the one that exhibits its effect on all the cells in our body. So, any dysfunction either reduced or increased has its effects on all the systems in our body. There are many studies in hypothyroidism and nervous system and only few studies done in patients with hyperthyroidism as neuropathy is found to be uncommon in hyperthyroidism. In contrary to neuropathy in hypothyroidism which is chronic and slowly progressing, the subjects present

with acute paralysis in hyperthyroidism. This study was carried out to evaluate the functional changes in peripheral nervous system in patients with hyperthyroidism by performing nerve conduction studies.

The prevalence of hyperthyroidism is found to be 2.77%, that is less than hypothyroidism which is around 4.2%. The usual clinical features of hyperthyroidism will be of increased appetite, weight loss, palpitations, Isolated Systolic Hypertension and in severe cases present with Arrhythmia. The neuromuscular problems like, myopathy, periodic paralysis, ophthalmoplegia and myasthenia gravis may be associated in toxic cases. The pathogenesis of neuropathy in hyperthyroidism is not well studied. It may be due to direct effect of increased level of thyroid hormones or immune mediated or due to increased metabolic rate, the nerve cells are depleted with essential nutrients. There may be microvascular changes in hyperthyroidism that affect the blood flow to the nerve fibers.

Neuromuscular involvement in the form of proximal myopathy with fasciculation is common in hyperthyroidism. There is no correlation between the degree of hyperthyroidism and myopathy. The serum levels of creatine kinase are not altered. Myopathy improves once hyperthyroidism is treated. Myasthenia gravis can occur in association with hyperthyroidism. Periodic paralysis occurring in hyperthyroidism resembles hypokalemic type of periodic paralysis. It sometimes occurs in the asymptomatic hyperthyroidism. In contrast to increased incidence of hyperthyroidism in females, this complication occurs more commonly in males. It is usually exacerbated by exercise or intake of high carbohydrate meals. It is more common in Asia. As it resembles hypokalemic type of periodic paralysis, acute attack usually responds to potassium supplementation. To prevent the repeated attack of this complication patient's thyroid status to be normalized.

Peripheral nervous system is also involved in hyperthyroidism. It takes the form of sensorimotor polyneuropathy. Peripheral neuropathy in combination with pyramidal tract involvement resembling amyotrophic lateral sclerosis is reported in one case. It has resolved by treatment with radioiodine. When the neuropathy involves lower limb it is termed as Basedow's paraplegia. Goiter does not always coexist with neuropathy in thyrotoxicosis. Hence routine thyroid function test is to be included in the investigations for neuropathy. Patients can present with confusion and agitation when associated with the thyroid storm. It can present as coma also.[1] Fisher M et al.[2] in their study have found out axonal degenerative changes in one patient with hyperthyroidism. This patient in addition, had involvement of corticospinal tract. It was completely corrected by $Iodine^{131}$ treatment Pooja Pothiwala et al.[3] found that proximal group of muscles are involved in periodic paralysis. It is more common in males. This is diagnosed when potassium level is reduced and the thyroid hormone level is increased. The complete remission can occur only when hyperthyroidism is corrected although acute episodes can be controlled by potassium supplementation. Out of seven patients diagnosed to suffer from familial periodic paralysis over a period of five years at Mayo's clinic, four patients had hyperthyroidism, a report by Harold F. Dunlap et al.[4]. Cesar H Magsino B et al[5] observed that hypokalemic periodic paralysis in some patients is preceeded by the intake of meal containing increased amount of carbohydrate[6]. They also noticed the increased incidence in men than women. Sensory system examination does not reveal any abnormality and patients are mentally normal. Drugs reducing the level of potassium like diuretics can also provoke an attack.

Ruurd F Duyff et al.[7] have done the nerve conduction study before and after treatment in both hypo and hyperthyroid groups. They have noticed the rapid and early occurrence of neuromuscular symptoms in hyperthyroid

group. The nerve conduction study after treatment has shown the complete resolution of neurological features in all hyperthyroid individuals and persisting abnormalities in some hypothyroid individual.

Aims and Objectives

To perform nerve conduction study in hyperthyroid female subjects and age matched controls and compare the results

MATERIALS & METHODS

This case control study was carried out at Tirunelveli Medical College Hospital after obtaining approval from the Institutional Ethics Committee. Newly diagnosed female patients with hyperthyroidism, aged between 20 and 50 years, were recruited. Age-matched healthy individuals were included as controls. The study comprised 18 patients with hyperthyroidism and 25 control subjects.

All participants were informed about the study protocol, and written informed consent was obtained prior to inclusion.

Exclusion criteria: Individuals with Diabetes Mellitus, Hypertension, previous neurological disorders, history of drug intake known to cause peripheral neuropathy, hepatic or renal disease, family history of neuropathy, and pregnant women were excluded from the study.

Detailed demographic data and clinical examination findings were recorded using a structured proforma.

Sensory nerve conduction studies were performed on the left median, left ulnar, and left sural nerves. Motor nerve conduction studies were carried out on the left median, left ulnar, and left posterior tibial nerves.

All nerve conduction studies were conducted using the RMS EMG EP MARK II system in the Neurophysiology Unit of the Department of Neurology. Surface electrodes were employed for recording. The filter settings were maintained at 2–10 Hz for motor studies and 2–3 Hz for sensory studies. Electrical stimulation was initiated at a low intensity and gradually increased until a maximal response was obtained.

RESULT

Following nerve conduction studies, the collected data from the study group and the control group were analysed and tabulated. The statistical analysis of the results was also undertaken. All the values obtained were expressed as mean $\pm$ S.D. The latency, conduction velocity, and action potential amplitudes for both motor and sensory nerves were recorded and analyzed. Statistical significance between groups were assessed using the unpaired Student's *t*-test using SPSS software 11.

Table 1 – Age Distribution of the Subjects

S. No	Age group in years	Hyperthyroid n = 18	Control n = 25
1	21-30	6	7
2	31-40	6	9
3	41-50	6	9
4	Mean Age	34.72	36.52
5	SD	8.75	8.10
6	p Value	0.49	-

***P value >0.05 not significant SD = standard deviation**

The study group consisted of 25 normal, and 18 hyperthyroid individuals. The mean age of the groups under study showed no significant difference when statistically compared.

Table 2 – Sensory Nerve conduction

	Nerve	Control	Hyperthyroid	P value
Latency (ms)	Ulnar	3.41 $\pm$ 0.19	3.67 $\pm$0.53	0.56
	Median	2.99 $\pm$ 0.19	3.58 $\pm$ 0.68	0.000*
	Sural	3.97 $\pm$ 0.26	4.77 $\pm$ 0.67	.000

Conduction Velocity (m/s)	Ulnar	51.09 ± 1.81	3.67 ±0.53	0.56
	Median	51.42 ±1.56	48.55 ± 2.18	0.000*
	Sural	42.20±1.86	40.52± 2.42	0.02*
SNAP (microvolt)	Ulnar	17.84 ± 0.67	16.7 ± 1.08	0.001*
	Median	21.35 ±1.39	18.88 ± 1.80	0.000*
	Sural	6.2 0± 0.41	5.4 ± 0.74	0.000*

***P value < 0.05 significant**

Table 2 shows the amplitude, conduction velocity and amplitude (SNAP) in left ulnar, median and sural nerve and it is compared with controls.

- The sensory conduction components of ulnar nerve showed significant decrease in the conduction velocity and amplitude. But no difference was observed in the latency in the hyperthyroid group as compared with controls.
- In hyperthyroid individual all the sensory conduction parameters of Median Nerve showed significant changes. Latency was increased and conduction velocity and amplitude were decreased than that of control group.
- The sensory conduction of sural nerve studied in the hyperthyroid group showed a statistically significant increase in the latency and a decrease in the amplitude of the action potential. This study did not show a significant difference in the conduction velocity in hyperthyroid patients.

Table-3 Motor Nerve conduction

Variable	Nerve	Control	Hyperthyroid	P value
Latency (ms)	Median	4.03 ± 0.35	4.16± 0.77	0.49
	Ulnar	2.99 ± 0.26	3.11 ± 0.29	0.181
	Tibial	5.82 ± 0.23	5.87 ± 0.46	0.66
Conduction Velocity (m/s)	Median	51.01 ±1.87	49.70±3.37	0.14
	Ulnar	51.14 ± 1.64	50.21± 1.65	0.078
	Tibial	43.46± 2.2	40.06 ± 1.64	0.000*
CMAP (milli volt)	Median	4.39 ± 0.26	4.05 ± 0.82	0.107
	Ulnar	6.23 ± 0.23	5.95±1.24	0.362
	Tibial	3.45 ±0.32	3.078± 0.66	0.038*

***P value <0.05 significant**

Table 3 shows the amplitude, conduction velocity and amplitude (CMAP) in left ulnar, median and posterior tibial nerve and it is compared with controls

- The conduction study of the posterior tibial nerve in hyperthyroid group showed significant reduction in amplitude and conduction velocity. The alteration in distal latency parameter was not significant.
- The distal latency, conduction velocity and CMAP of motor conduction study of Median Nerve and Ulnar Nerve did not exhibit a significant change in hyperthyroid group as compared to control group

Table -4 F wave Latency

Nerve	Control	Hyperthyroid	P value
Tibial	47.26± 0.69	47.50±0.61	0.24
Median	24.1± 0.75	23.96±0.86	0.60
Ulnar	25.46±0.64	25.34±0.61	0.55

P value > 0.05 not significant

Table 4 shows F wave latency compared with hyperthyroid and control subjects.

There was no significant change in F wave latency in hyperthyroid group as compared to control.

Table 5 Neuropathy in Hyperthyroidism

Neuropathy	No of Hyperthyroid	Percentage
Sensory	11	61.1
Sensorimotor neuropathy	1	5.5
Carpal tunnel syndrome	3	16.6

Table 5 shows that 61.1 % of patient had sensory neuropathy and 5.5 % and 16.6% of patients were affected by sensorimotor neuropathy and entrapment neuropathy in the form of carpal tunnel syndrome respectively.

DISCUSSION

In the present study, the nerve conduction study was performed in 18 hyperthyroid, and 25 control subjects. The diagnosis of peripheral neuropathy is made if two or more nerves are involved. Prolonged latency in sensory conduction study indicates sensory neuropathy. In motor conduction study, decrease in amplitude denotes axonal degeneration and prolonged distal latency and conduction velocity indicate demyelination. Carpal tunnel syndrome is indicated by the significant prolongation of distal latency.

Hyperthyroidism is common in females and is also most commonly due to autoimmune disorders and is slowly progressive over a period of time. The present author had observed a significant prolongation of latency of the sensory conduction of the median and sural nerve. This finding is similar to the observations made by Ihsan[8] M. Ajeena et al. Gulbun Yuskel[9] and Berlit et al.[10] in their study found the sural nerve latency changes as in our study but not in favour of changes in the Median Nerve Latency. Latency of sensory conduction of ulnar nerve showed no significant results. This finding is significantly similar to most of the study.

Motor nerve conduction study was performed in posterior tibial, median and ulnar nerve in our study. Analysing the results of motor nerve conduction only posterior tibial nerve showed significant reduction in amplitude and conduction velocity and median and ulnar nerve parameters are not showing significant findings. These findings are similar to study by Ihsan M.Ajeena et al, who has seen no significant changes in Median and Ulnar Nerve parameters. Gulbun Yuskel[9] et al have found out a significant reduction in conduction velocity in Tibial nerve study as that of our study.

The predominant involvement of sensory than motor nerve in hyperthyroidism has been reported in the literature by Ruurd F Duyff[7]. The predominant and early sensory nerve involvement may be due to long axons in sensory nerves, and they have less metabolic reserve. No significant change in F wave latency in any of the nerve was noted in our study. Many authors agree with this finding. Longer duration of the symptoms in most of the patients of the hyperthyroid group is a probable reason for involvement of Tibial nerve.

To summarise, the present study had found the presence of sensory neuropathy in 61 %, sensory motor neuropathy in 5.5% and carpal tunnel syndrome in 17 % of hyperthyroid individuals. Ihsan M. Ajeena et al agree with the incidence of sensorimotor neuropathy. The incidence of carpel tunnel syndrome and sensorineuropathy is comparable with the study by Hala et al. The state of increased basal metabolic rate in hyperthyroidism is the proposed hypothesis for axonal type of polyneuropathy.

CONCLUSION

There is significant nerve involvement in Hyperthyroidism patients. The neuropathy predominantly affects sensory nerve compared to Motor Nerve. The study emphasizes the need to include Nerve Conduction Study as a routine in patients with hyperthyroidism as there is significant neural involvement in them and may present as an acute event.

Declaration by Authors
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