

Sensory Neuropathy in Hypothyroidism : Electrophysiological and Clinical Findings

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Peripheral neuropathy may be a manifestation of hypothyroidism which usually develops insidiously over a long period of time due to irregular taking of drugs or lack of thyroid hormone replacement. The present study was designed to observe the clinical and electro-physiological findings in hypothyroid patients in order to evaluate the neuromuscular dysfunction as well as sensory neuropathy. For this purpose, 70 subjects with the age range of 20 to 50 years of both sexes were included in the study. Among them, 40 hypothyroid patients were taken in study group (Group B) and 30 apparently healthy subjects were taken as control (Group A). On the basis of their TSH levels, group B was further divided into group B₁ with TSH <60 MIU /L or (less severe) and group B₂ with TSH >60 MIU /L (severe group). The duration of the disease ranged from 6 months to 5 years. All the hypothyroid patients were selected from Thyroid Clinic, Center of Nuclear Medicine and Ultra sound, Dhaka Medical College and Hospital, Dhaka, during the period from January 2005 to December 2005. Healthy subjects were selected from personal contact. Most of the hypothyroid patients were under hormone replacement therapy. Diagnosis of hypothyroidism was done by serum levels of TT₃, TT₄ and the TSH.

In this study, both TT₃, TT₄ levels were significantly (P<0.01) lower in hypothyroids in comparison to those of control. The patients were searched for the clinical signs of sensory neuropathy. Clinical findings revealed diminished or absence of most of the deep tendon reflexes. The nerve conduction studies for sensory nerve function were done in all the subjects by electrophysiological technique. All the tests were done in median and ulnar nerve for upper limb and in sural nerve for lower limb and these parameters were measured on the day 1 (one) of their first visit. Data were compared among the different groups. Most of the patients had higher sensory distal latencies (SDL) with lower conduction velocities (SNCV) which were more marked in severe cases. About 67.5% of hypothyroid patients had shown abnormal sensory NCV when compared to that of euthyroids. Therefore, this study concludes that sensory neuropathy may be a consequence of hypothyroidism.

Key Words: Hypothyroidism; Neuropathy; Electrophysiology

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Introduction

Hypothyroidism is a clinical condition associated with low levels of thyroid hormones with raised TSH. It may be due to some intrinsic disorders in thyroid or may be disorder in pituitary or hypothalamus.¹⁻³

Different investigators studied nerve conduction parameters in patients suffering from hypothyroidism to observe the incidence of neuropathy and functional status of peripheral nerves in thyroid deficiency.⁴⁻⁶ In their study, most of them had shown that deficiency of

thyroid hormones cause sensory neuropathy by affecting different peripheral nerves but more commonly the median nerve. The common nerve conduction parameters done by the investigators include sensory distal latencies (SDL), sensory conduction velocities (SNCV) in different peripheral nerves. The increased SDL and decreased SNCV in any nerve indicate sensory conduction impairment of that nerve. The sensory nerve conduction impairment is frequent in early stage of neuropathy in thyroid deficiency and the common complaints are usually pain, cramps, paraesthesia of fingers and limbs. So, this group of patients is usually manifested by the features of Carpal Tunnel Syndrome and sometimes of Tarsal Tunnel Syndrome.⁴⁻⁶

In our country, a good number of patients are suffering from thyroid deficiency which varies from mild to its severe form.⁷ As most of the patients were illiterate and of low socioeconomic status, they were not aware about the consequences as well as the complications of delayed or irregular treatment.

Again, severity of thyroid deficiency may have some relationship with the occurrence of neuropathy²; they need to be more conscious about complications of the disease. Though a few published data regarding the normal values of nerve conduction parameters of healthy Bangladeshi population are available,⁸ no data has yet to be reported in hypothyroid patients on these aspects.

Therefore, the study has been designed to find out the sensory nerve conduction status of some peripheral nerves in order to evaluate presence of sensory neuropathy in hypothyroid patients.

The study also aimed at to give a guideline to the physicians for proper and better management of hypothyroids and also to create awareness among this group of patients so that they can take early and regular treatment and thereby minimizes the occurrence of the peripheral neuropathy in hypothyroids.

Methods

The present observational study was carried out in department of physiology, BSMMU, Dhaka from January 2005 to December 2005. In this study, a total number of 70 subjects with the age range of 20 to 50 years of both sexes were included, of whom 30 euthyroids (TSH=0.3-5MIU/L) were included in group A (control) and 40 hypothyroids were included in group B (study group). On the basis of TSH levels, they were further divided into group B₁ considered less severe group with TSH < 60 MIU/L with 15 hypothyroids and group B₂ as severe group with TSH > 60 MIU/L with 25 hypothyroid patients. Most of the patients were treated by thyroid hormones.

The duration of the disease was from 6 months to 5 years. The objectives of the study were explained to each of the subjects and their written consents were taken. Detailed medical history regarding drug intake was taken and general examinations were done. The common features of sensory nerve dysfunctions like pain, cramps, paraesthesias of fingers and limbs were searched for in all patients and all the information were documented in the data sheet. The hormones were measured by RIA^{9, 10} for TT₃ and TT₄ and IRMA¹¹ for TSH. The nerve conduction studies were done by electrophysiological method with a standard NCV machine¹²⁻¹³.

The statistical analysis was done by one way ANOVA and z test. The study was performed at room temperature.

Results

All the parametric variables were expressed as mean (\pm SD) except the TSH levels.

The comparison of the values was done among the different groups. In this study, the mean TT₃ and TT₄ were significantly lower in hypothyroids in comparison to those of healthy group but it was not statistically significant (Table I).

Table – I : The serum of TT₃ and TT₄ and TSH levels of the study subjects (n=70)

Groups	TT ₃ (nmol/L)	TT ₄ (nmol/L)	TSH (MIU/L)
A (n=30)	2.18 ± 0.53 (1.40-3.02)	129 ± 28.51 (71.19-172)	0.76-4.8
B ₁ (n=15)	1.31 ± 0.81 (1.3-2.7)	61.21 ± 29.81 (40-170)	7-<60
B ₂ (n=25)	1.10 ± 0.85 (0.45-1.25)	54.4 ± 39.31 (21-165)	>60
Statistical analysis			
Groups	P Value		
A vs. B ₁	<0.01**	<0.001***	
A vs. B ₂	<0.001***	<0.001***	
B ₁ vs B ₂	0.75 ^{NS}	0.889 ^{NS}	

Results are expressed as Mean ± SD; One-way ANOVA (with Post Hoc Tests) was performed as the test of significance. Figures in the parentheses indicate the ranges.

Group A=Euthyroids (control group),
Group B₁=Hypothyroids with TSH level <60 MIU/L,
Group B₂=Hypothyroids with TSH level >60 MIU/L,
***= P < 0.001, **= P < 0.01.
n=Number of subjects, NS=Not significant.

The typical clinical features of neuropathy were absent in all hypothyroid patients except diminished or absence of most of the deep tendon reflexes.

Nerve study in median nerve revealed, (Table II).significantly higher distal latency (SDL) and lower conduction velocity (SNCV) in both of the hypothyroid groups in comparison to those of the control except the SNCV in group B₁ (less severe).

On the other hand, for ulnar nerves (Table III) the differences of these values were statistically significant between euthyroids (group A) and severe hypothyroids (group B₂) but not with the less severe hypothyroids (group B₁).

Table - II : Nerve conduction parameters for sensory function of Median nerve (n=70).

Group	M d latency (msec)	M NCV (m/sec)
A (n=30)	2.11 ± 0.305 (1.70 – 2.60)	54.67 ± 3.853 (50.00 – 61.00)
B ₁ (n=15)	2.53 ± 0.586 (2.00 – 3.60)	48.27 ± 5.257 (38.00 – 58.00)
B ₂ (n=25)	2.60 ± 0.635 (1.90 – 4.20)	48.04 ± 6.604 (38.00 – 58.00)

Results are expressed as Mean (±Standard deviation); One way ANOVA (Post Hoc Tests) was performed as the test of significance, The figures in parentheses indicate ranges.

Group A =Euthyroid control Group,
Group B₁ = Hypothyroids with TSH level < 60 m IU/L,
Group B₂ = Hypothyroids with TSH level > 60 m IU/L, M d latency = Median Distal Latency, M NCV = Median Nerve Conduction Velocity, *** = P < 0.001, ** = P < 0.01,
= < 0.05. n = Number of subjects, NS = Not Significant.

Table – III : Nerve conduction parameters for sensory function of Ulnar nerve (n=70).

Group	U d latency (msec)	U NCV (m/sec)
A (n=30)	2.15 ± 0.357 (1.70 – 3.10)	56.10 ± 5.235 (48.00 – 65.00)
B ₁ (n=15)	2.38 ± 0.578 (1.70 – 3.20)	52.47 ± 3.998 (43.00 – 57.00)
B ₂ (n=25)	2.68 ± 0.878 (1.50 – 4.80)	47.28 ± 10.454 (21.00 – 63.00)

Statistical Analysis

Group	P value	
A vs. B ₁	0.594 ^{NS}	0.325 ^{NS}
A vs. B ₂	<0.01**	<0.001***
B ₁ vs. B ₂	0.375 ^{NS}	0.100 ^{NS}

Results are expressed as Mean (± Standard deviation); One-way ANOVA (Post Hoc Test) was performed as the test of significance. The figures in parentheses indicate the ranges.

Group A =Euthyroid control group,
Group B₁ = Hypothyroids with TSH level < 60 m IU/L,
Group B₂ = Hypothyroids with TSH level > 60 m IU/L, U d latency = Ulnar Distal Latency, U NCV = Ulnar Nerve Conduction Velocity, *** = P < 0.001,
** = P < 0.01, n = Number of subjects, NS = Not Significant.

For sural nerve, similar findings were also observed but the differences of these values were statistically significant between euthyroids (group A) and all the hypothyroids but not between group B₁ and group B₂. (Table IV).

Table-IV : Nerve conduction parameters for sensory function of Sural nerve (n=70).

Group	S d latency (msec)	S NCV (m/sec)
A (n=30)	2.46 ± 0.227 (2.00 – 2.70)	53.46 ± 3.319 (46.00 – 61.00)
B ₁ (n=15)	4.01 ± 0.898 (2.70 – 6.50)	39.73 ± 6.452 (22.00 – 47.00)
B ₂ (n=25)	3.88±1.315 (1.70 – 6.50)	41.80±10.531 (22.00 – 57.00)
Statistical Analysis		
Group	P value	
A vs. B ₁	<0.001 ***	
A vs. B ₂	<0.001 ***	
B ₁ vs. B ₂	0.957 NS	

Results are expressed as mean (± standard deviation); one way ANOVA (Post Hoc Tests) was performed as the test of significance. The figures in parentheses indicate ranges.

Group A = Euthyroid control group,

Group B₁ = Hypothyroids with TSH level < 60 m IU/L,

Group B₂ = Hypothyroids with TSH level > 60 m IU/L,

S d latency = Sural distal latency, S NCV = Sural nerve conduction velocity, *** = P < 0.001, n = Number of subjects,

NS = Not significant.

On the other hand, all the parameters between two hypothyroid groups were statistically non significant.

Again, in the present study 67.5% of the hypothyroid subjects showed abnormal NCV. Among them, 66% of the subjects were in severe group and 34% in less severe group (Table-V).

The SNAP and CMAP were not measured due to very little changes in the amplitude.

Table – V : Distribution of subjects by NCV (n=70)

Groups	n	Normal NCV		Abnormal NCV	
		n	(%)	n	(%)
A	30	27	90	3	10
B	40	13	32.5	27	67.5 ***
B ₁	15	6	40	9	60
B ₂	25	7	28	18	72

Statistical analysis was done by 'Z' test .

Z = 6.243, ***=P<0.001.

Group A=Euthyroid (control) group,

Group B= Hypothyroid group,

Group B₁=less severe hypothyroids,

Group B₂ =Severe hypothyroids,

n=Number of subjects, NCV=Nerve conduction velocity.

Discussion

In this study, All the hypothyroids had significantly (P < 0.01) lower TT₃ and TT₄ levels compared to euthyroids.

The hypothyroid patients showed no remarkable clinical signs of neuropathy with the exception of few like diminished or absence of most of the deep tendon reflexes.

In this study a significant number of hypothyroid patients showed nerve conduction abnormalities by electrophysiological examination. However, the nerve conduction parameters in the control group were similar or nearer to normal reference values .^{12, 13, 4,,9,-.11}

Some groups of investigators of different countries had also observed the slowing of nerve conduction velocities in different peripheral nerves but they did not mention about the individual values of the parameters like sensory distal latency (SDL) and sensory nerve conduction velocity (SNCV).^{5-6,14- 16}

Both the hypothyroid groups showed significantly higher sensory distal latencies (SDL) with lower sensory nerve conduction

velocities (SNCV) for median, ulnar and sural nerves. Again, the nerve conduction study revealed the predominant impairment in the sural nerve among the three nerves as the differences of all the parameters were statistically significant between euthyroids and both the less severe and severe hypothyroids for sural nerve. However, the investigators of different countries mentioned about the involvement of median nerve.^{1,5-6,9,14-16}

The mechanism involved in the development of neuropathy in hypothyroidism is not yet fully cleared but different investigators proposed that the weight gain may be a contributory factor for neuropathy. In addition, the deposition of mucopolysaccharide or the myxedematous tissue may also lead to compression over the peripheral nerves and thereby results in swelling and degeneration of those nerves^{4,6}

Under normal physiological condition, thyroid hormone is responsible for the stimulation of mitochondrial respiratory activity to produce energy in the form of ATP. Hormones seem to increase ATPase activity and consequently ATP dependent Na^+/K^+ pump. Therefore, in hypothyroidism ATP deficiency and reduce ATPase activity with decreased Na^+/K^+ pump activity cause subsequent alteration of pump dependent axonal transport and thereby may leads to peripheral neuropathy¹⁴. Decrease glycogen degradation may also leads to energy deficit in hypothyroidism^{5-6,14-16}. Though the neuropathy due to compression and the peripheral neuropathy due to axonal degeneration are not fully distinguished, most likely that there may be a combination of both these two factors, which results in the development of peripheral as well as the sensory neuropathy in hypothyroidism⁴.

Therefore, this study revealed that sensory neuropathy is common manifestation in patients suffering from hypothyroidism in our population.

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