Motor conduction parameters in recently diagnosed and untreated hypothyroidism

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KEY WORDS
Hypothyroidism
Neuropathy
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ABSTRACT

Background: The severity of neuromuscular symptoms and signs in hypothyroidism is known to be related to the duration and degree of hormone deficiency.

Purpose: The present study was aimed to assess whether recently diagnosed and untreated hypothyroidism affects peripheral nervous system.

Methods: The study included a total of 120 female subjects with age ranging from 20 to 45 years. The motor nerve conduction parameters viz. Distal latency (DL), amplitude of compound muscle action potential (CMAP) and motor nerve conduction velocity (MNCV) were recorded bilaterally in median, ulnar and posterior tibial nerves using standard protocols and settings.

Results: The observations revealed significantly prolonged distal motor latencies, reduced CMAP amplitudes and slowed MNCV in the peripheral nerves in hypothyroidism.

Conclusion: The results indicated that the alteration in motor conduction parameters in recently diagnosed and untreated hypothyroidism might be due to various functional and structural changes in peripheral nerves associated with deficiency of thyroid hormones.

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Introduction

The normal growth and development of an individual is profoundly influenced by the thyroid hormones. Though thyroid hormones are not essential for maintenance of vital functions of life, their deficiency causes severe deficit in mental and physical growth and extreme decrease in body metabolism.1

As per Indian Thyroid Society (ITS), around 42 million people in India suffer from diseases related to thyroid gland, hypothyroidism being the most prevalent disorder affecting one in every eight women. Women are 5–8 times more susceptible to the disease.2 Although hypothyroidism affects almost all systems of the body, these patients often have symptoms and signs of neuromuscular dysfunction. The prevalence of neurological complications have been reported to be around 79% in hypothyroidism.3

Nerve conduction study (NCS) is an electrodiagnostic technique to study functional status of the peripheral nerves and establish the type and degree of abnormalities of the nerves. It is now widely used, not only for the precise localization of neural lesions, but also for the accurate characterization of the peripheral nerve functions. The technique consists of an electrical stimulation of somatic nerves and the recording of the evoked potentials, either from the muscles or from the nerves themselves. Thus structural as well as functional changes in the nerves can be evaluated by these nerve conduction studies early and accurately in the course of the neural disease.4

As claimed by ITS, a good number of individuals are suffering from mild to severe deficiency of thyroid hormones in India. Most of the patients are not aware about the consequences as well as complications of delayed or irregular treatment. The published data regarding studies on nerve conduction para-

Conclusion

As neuromuscular dysfunction may be associated with hypothyroidism, the nerve conduction parameters are expected to be altered in these patients. Therefore, the present study was intended to assess various motor conduction parameters in recently diagnosed and untreated hypothyroid patients and compare them with that of normal healthy controls.

Methods

The present study was designed as a case-control study and conducted at Indira Gandhi Govt. Medical College and Hospital, Nagpur. Before commencement, the project was duly approved by the Ethics Committee of the Institution. Informed consent was obtained from all the subjects after explaining them the study protocol.

The subjects in the study were grouped as:

1. Hypothyroid (study group), n = 60
2. Euthyroid (control group), n = 60

Hypothyroid group included a total of 60 female subjects with age ranging from 20 to 45 years, recently diagnosed as having hypothyroidism (either TSH raised above normal with total T4 and total T3 within normal range or raised TSH with below normal T4 and T3)3,5,6 and were not started with hormone replacement therapy. These subjects were selected from Out Patient Department of the Institution.

For comparison, a group of healthy females belonging to the same age group with similar height, dietary habits and ethnicity, as hypothyroid group, was included in the control group. These controls were not having any known or diagnosed illness
and their thyroid profiles were within normal range. All the subjects in the present study belonged to the same socio-economic status. The subjects with any history pertaining to the conditions other than hypothyroidism and moderate to long term exposure to the drugs or chemicals, which can lead to neuropathy, were excluded from the study.

The diagnosis of hypothyroidism was made by using Microwell ELISA technique with ERBA Thyrokot from ERBA Diagnostics Manheim GMBH, Germany. The normal values of the hormones according to the laboratory kits were considered as follows:

\[
TSH = 0.44 - 3.45 \mu IU/ml, \quad T_4 = 5.3 - 12.1 \mu g/dL \text{ and } \quad T_3 = 0.51 - 1.58 \text{ ng/ml.}
\]

After taking detailed history with a set of screening questions referring to principal symptoms of thyroid disease, thorough clinical examination was done. Special attention was given to the detailed neurological examination including cranial nerves. Reflexes were elicited and ankle jerk was particularly examined. Motor conduction studies were done bilaterally on Median, Ulnar and Posterior Tibial nerves with respect to distal latency (DL), Amplitude of the compound muscle action potential (CMAP) and the motor nerve conduction Velocity (MNCV).

The recording procedure

A complete NCS was done in all the subjects with RMS-EMG-EP Mark II using standard protocols and settings. 1-cm disc surface electrodes were used with surface stimulators. Three types of electrodes were used i.e. active, reference and ground. The ground electrode served as a zero voltage reference point.\(^7\) The temperature of the examination room was maintained at about 25–28°C.\(^4\) The subject was taken to the room, rested for a while so as to decrease the skin temperature to the recommended level of 32–34°C. Thereafter, the NCS procedure was carried out on the subject lying comfortably in supine position on the bed.\(^5\)

The motor conduction parameters in the median nerve (motor to abductor pollicis brevis) were recorded by placing electrodes and stimulators on the hand and forearm,\(^4,6\) as follows: the active electrode was placed halfway between the midpoint of distal crease and the first metacarpophalangeal joint. The reference electrode was placed slightly distal to the first metacarpophalangeal joint. The ground electrode was placed on the dorsum of the hand. The machine settings for recording the parameters in the median nerve were same as that for the median nerve. Then the nerve was stimulated by placing the cathode of the stimulator 8 cm proximal to active electrode (stimulation point 1) with anode directed proximally. The record i.e. the CMAP was obtained in the same manner as for median nerve and was saved. The nerve was again stimulated with the same settings by placing the cathode of the stimulator approximately 4 cm distal to the medial epicondyle (stimulation point 2) with anode directed proximally. Again, the record was obtained on the monitor and was saved. The values of the distal latency and the amplitude of CMAP were obtained from the monitor and the MNCV was calculated in similar manner to that of median nerve.

With the subject in supine position, the motor conduction parameters in the posterior tibial nerve (motor to abductor hallucis longus) were recorded by placing the electrodes and the stimulators on the foot,\(^4,6\) as follows: the active electrode was placed at medial foot. The reference electrode was placed slightly distal to the first metatarsophalangeal joint. The ground electrode was placed at the dorsum of the foot. The machine settings for recording the parameters in the posterior tibial nerve were same as that for the median nerve. Then the nerve was stimulated by placing the cathode of the stimulator 8 cm proximal to the active electrode (stimulation point 1) with anode placed proximally to cathode. The record i.e. CMAP was obtained in the same manner as for median nerve and was saved. The nerve was again stimulated with the same settings by placing the cathode of the stimulator at the medial popliteal fossa (stimulation point 2) with anode directed proximally. Again, the record was obtained on the monitor and was saved. The distal latency and the amplitude of CMAP were obtained from the monitor. The MNCV was measured in the same manner as that of median nerve.

All these electrophysiological parameters in the median nerve, ulnar nerve and the posterior tibial nerve were recorded bilaterally in all the subjects and finally expressed as mean with standard deviation. These values of each parameter in the hypothyroid group and the control group were compared and analyzed using unpaired students t test. P value less than
### Table 1: Comparison and analysis of various anthropometric and thyroid profile parameters in control and hypothyroid

| Variable       | Control (n = 60) Mean ± SD | Hypothyroid (n = 60) Mean ± SD | P value |
|----------------|----------------------------|-------------------------------|---------|
| Age (years)    | 32.41 ± 8.04               | 32.53 ± 7.60                 | 0.93<sup>NS</sup> |
| Height (cm)    | 157.57 ± 2.04              | 157.80 ± 2.12                | 0.55<sup>NS</sup> |
| Weight (kg)    | 52.57 ± 1.95               | 53.49 ± 1.65                 | <0.05<sup>*</sup> |
| BMI (kg/m²)    | 21.17 ± 0.69               | 21.49 ± 0.80                 | <0.05<sup>*</sup> |
| TSH (µIU/ml)   | 3.20 ± 0.30                | 3.86 ± 0.31                  | <0.05<sup>*</sup> |
| T<sub>4</sub> (µg/dL) | 5.30 ± 0.43               | 5.00 ± 0.58                  | <0.05<sup>*</sup> |
| T<sub>3</sub> (ng/ml) | 0.57 ± 0.18               | 0.45 ± 0.26                  | <0.05<sup>*</sup> |

SD: standard deviation, *: statistically significant, NS: statistically nonsignificant.

### Table 2: Comparison and analysis of various motor conduction parameters of Median nerve in control and hypothyroid

| Variable       | Nerve       | Control (n = 60) Mean ± SD | Hypothyroid (n = 60) Mean ± SD | P value |
|----------------|-------------|----------------------------|-------------------------------|---------|
| DL (msec)      | Right nerve | 2.97 ± 0.44                | 3.91 ± 0.84                   | <0.05<sup>*</sup> |
|                | Left nerve  | 2.84 ± 0.65                | 3.92 ± 0.79                   | <0.05<sup>*</sup> |
| CMAP amplitude (mV) | Right nerve | 4.36 ± 0.62                | 3.99 ± 0.66                   | <0.05<sup>*</sup> |
|                | Left nerve  | 4.62 ± 0.42                | 4.27 ± 0.77                   | <0.05<sup>*</sup> |
| MNCV (m/sec)   | Right nerve | 58.12 ± 4.21               | 55.59 ± 4.55                  | <0.05<sup>*</sup> |
|                | Left nerve  | 58.85 ± 4.60               | 54.90 ± 5.07                  | <0.05<sup>*</sup> |

SD: standard deviation, *: statistically significant, DL: distal latency, CMAP: compound muscle action potential, MNCV: motor nerve conduction velocity.

### Table 3: Comparison and analysis of various motor conduction parameters of Ulnar nerve in control and hypothyroid

| Variable       | Nerve       | Control (n = 60) Mean ± SD | Hypothyroid (n = 60) Mean ± SD | P value |
|----------------|-------------|----------------------------|-------------------------------|---------|
| DL (msec)      | Right nerve | 2.69 ± 0.25                | 3.00 ± 0.67                   | <0.05<sup>*</sup> |
|                | Left nerve  | 2.56 ± 0.36                | 2.89 ± 0.68                   | <0.05<sup>*</sup> |
| CMAP amplitude (mV) | Right nerve | 6.38 ± 0.70                | 6.08 ± 0.62                   | <0.05<sup>*</sup> |
|                | Left nerve  | 6.33 ± 0.25                | 6.11 ± 0.52                   | <0.05<sup>*</sup> |
| MNCV (m/sec)   | Right nerve | 59.86 ± 4.80               | 57.34 ± 5.20                  | <0.05<sup>*</sup> |
|                | Left nerve  | 60.17 ± 4.93               | 56.70 ± 4.90                  | <0.05<sup>*</sup> |

SD: standard deviation, *: statistically significant, DL: distal latency, CMAP: compound muscle action potential, MNCV: motor nerve conduction velocity.

### Table 4: Comparison and analysis of various motor conduction parameters of Posterior Tibial nerve in control and hypothyroid

| Variable       | Nerve       | Control (n = 60) Mean ± SD | Hypothyroid (n = 60) Mean ± SD | P value |
|----------------|-------------|----------------------------|-------------------------------|---------|
| DL (msec)      | Right nerve | 3.09 ± 0.54                | 3.39 ± 0.80                   | <0.05<sup>*</sup> |
|                | Left nerve  | 3.12 ± 0.52                | 3.38 ± 0.95                   | 0.0613<sup>NS</sup> |
| CMAP amplitude (mV) | Right nerve | 4.84 ± 0.76                | 4.46 ± 0.81                   | <0.05<sup>*</sup> |
|                | Left nerve  | 4.93 ± 0.85                | 4.67 ± 0.69                   | 0.0665<sup>NS</sup> |
| MNCV (m/sec)   | Right nerve | 44.52 ± 2.57               | 41.91 ± 4.78                  | <0.05<sup>*</sup> |
|                | Left nerve  | 44.53 ± 2.34               | 38.74 ± 4.49                  | <0.05<sup>*</sup> |

SD: standard deviation, *: statistically significant, NS: statistically nonsignificant, DL: distal latency, CMAP: compound muscle action potential, MNCV: motor nerve conduction velocity.
0.05 was considered as an indicator of statistically significant difference between the compared values.

**Results**

Table 1 depicts mean and standard deviation of various anthropometric and thyroid profile parameters in control and hypothyroid. Tables 2, 3 and 4 depict mean and standard deviation of motor conduction parameters in bilateral Median, Ulnar and Posterior Tibial nerves respectively. These tables also show p values and results of t tests for comparison between control and hypothyroid.

The differences in age and height of control and hypothyroid were found to be statistically non-significant (Table 1).

Weight and BMI were found to be increased in hypothyroid as compared to that of control. This increase in weight and BMI of hypothyroid was statistically significant (Table 1).

TSH level in hypothyroid was found to be elevated as compared to that of control. This elevation was statistically significant. The levels of T4 and T3 in hypothyroid were found to be decreased as compared to that of control and the difference was statistically significant (Table 1).

The distal latency was found to be delayed in all the nerves under consideration in hypothyroid as compared to that of control. This delay was statistically significant except for left posterior tibial nerve (Tables 2, 3 and 4).

The amplitude of compound muscle action potential was found to be reduced in all the nerves in hypothyroid as compared to that of control and it was statistically significant except for left posterior tibial nerve (Tables 2, 3 and 4).

The motor nerve conduction velocity was found to be attenuated in all the nerves of hypothyroid as compared to that of control. This slower conduction was statistically significant (Tables 2, 3 and 4).

**Discussion**

In the present study, the comparison of age and height of control and hypothyroid did not reveal any significant difference. This suggests that the groups were age and height matched. The study also showed that the hypothyroids had statistically significant increased weight and BMI as well as altered motor nerve conduction parameters as compared to that of control.

The increased weight in hypothyroids might be due to accumulation of mucopolysaccharides, hyaluronic acid and chondroitin sulphate in the interstitial spaces which, because of their hydrophilic nature, retain water along with them resulting in weight gain. Although the BMI was increased in hypothyroid, the increment was within normal range. It indicates the absence of true obesity in them. These findings related to weight and BMI are consistent with that of Kasper DL et al 2005 and Sabina Y et al 2008.

Hypothyroid showed significantly prolonged distal motor latencies, reduced CMAP amplitudes and slowed MNCV for bilateral median, ulnar and posterior tibial nerves. These findings for motor conduction parameters in hypothyroids are consistent with that reported by Kcececi H et al 2006, El-Salem K et al 2006 and Sabina et al 2008.

The mechanisms involved in the development of neuropathy in hypothyroidism are not yet fully established. The neurological dysfunction associated with hypothyroidism may be a result of hormonal imbalance or may be related to the immune mechanisms associated with thyroid diseases. Some investigators suggested that the weight gain in the hypothyroids may be a contributory factor for neuropathy. In addition, the deposition of mucopolysaccharides in the tissues surrounding the nerves or the myxedematous tissue may also lead to compression over the peripheral nerves there by resulting in swelling and degeneration of the nerves. A similar mechanism of nerve damage has been postulated for peripheral neuropathy in carpal tunnel syndrome. The median nerve entrapment at the wrist caused by the deposition of mucinous material in the tissues surrounding the nerve is one of the most frequent causes of peripheral nerve damage in hypothyroidism.

The thyroid hormones stimulate the mitochondrial respiratory activity to produce energy in the form of ATP during aero-biosis under normal physiological conditions. Hypothyroidism leads to energy deficit due to decreased oxidation of nutrients. Decreased degradation of glycogen leads to formation of glycogen deposits around the nerves. These metabolic alterations induced by hypothyroidism may initially damage the functions and later on induce structural changes in the nerves.

The thyroid hormones also increase the ATPase activity and consequently Na-K pump activity in normal individuals. Therefore, the deficiency of ATP, reduced ATPase and Na-K pump activity in hypothyroidism cause subsequent alteration of pump dependent axonal transport and may lead to peripheral neuropathy. The peripheral nerve dysfunction was also linked to the morphological evidence of primary axonal degeneration in the form of shrinkage of axons, disintegration of neurotubules and neurofilaments and active axonal breakdown. Some investigators studied the patients of hypothyroidism morphologically and neurophysiologically and suggested that the metabolic alterations caused by hypothyroidism were responsible for the peripheral neuropathy. However, the neuropathy due to compression and that due to axonal degeneration are not fully distinguished. There may be a combination of both of these which results in the development of peripheral neuropathy in hypothyroidism.

The motor neural dysfunction seen in the present study may be linked to the various functional and structural changes in peripheral nerves associated with deficiency of thyroid hormones.

**Conclusion**

Our study confirms the involvement of peripheral nerves in hypothyroidism. In adults, as the hypothyroidism has insidious onset, diagnosis can be delayed by months or years and the neuropathic manifestations can go unrecognized for longer period. Therefore, performing electrophysiological studies in hypothyroid patients is suggested, early in the course of the disease in order to detect nervous system involvement. Further research is needed to see whether the neurological dysfunction in hypothyroidism is reversible with the appropriate hormone replacement therapy.

**Authorship contributions**

Ashwini A Mahadule: Collection of data, statistical analysis and drafting of article, Pravin S Jadhao: Design of study and statistical analysis, Mrunal S Phatak: Raising the article to intellectual level.
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