Nerve Conduction Study in Early Diagnosed Cases of Hypothyroidism in Central India

Komal Meshram[1], Alka Rawekar[2], Ajay Meshram[3], Harshwardhan Meshram[4], Anjali Vaggha[5], Shilpa Ingle[6]

[1]Associate Prof, Dept Physiology, DMMC, Wanadongri, Nagpur, [2]Prof, Dept Physiology, DMIMSU (DU) Sawangi, Wardha, [3]Prof Dept Biochemistry, DMIMSU (DU) Sawangi, Wardha, [4]3rd Year MBBS Student LTMMC, Sion, Mumbai, [5]Assistant Prof, Deptbiochemistry, DMIMSU (DU) Sawangi, Wardha, [6]Assistant Prof, Dept Pharmacology, PDMC, Amravati

Abstract

Thyroid gland has multiple effects on the neuromuscular system and brain, its dysfunction is associated with characteristic symptoms and signs with functional alterations in many organs and systems. Thyroid disease may cause signs and symptoms of neuromuscular dysfunction. Hypothyroidism has been associated with the clinical features of proximal muscle weakness, mononeuropathy and sensorimotor polyneuropathy.Nerve conduction studies (NCS) are useful adjunct to the clinical examination of the peripheral nervous system as it is helpful to test speed of signals through a nerve. They help to delineate the extent and distribution of the neural lesion and distinguish two major categories of peripheral nerve disease demyelination and axonal degeneration. Present cross sectional studywas conducted at Central Neurophysiology Laboratory in tertiary care teaching hospital, J.N.M.C, Sawangi (M), Wardha catering to rural population of central India to assess the nerve conduction in early diagnosed hypothyroid patients. Total twenty seven patients; 20-50yrs of age were screened for nerve conduction.In our study we got mixed type of peripheral neuropathy. Out of 27 patients with age 18-30 yrs- 1(16.67%), 31-40 yrs- 13(61.90%) and 41-50 yrs -7 (33.3 %) had abnormal NCS. Occurrence of neuropathy was more common in female patients 80.95% as compared to male patients 19.05%.Sensory nerve action potential (SNAP) amplitudes and conduction velocity were significantly reduced ($p<0.05$) in cases diagnosed as hypothyroidism in median (77%), sural (70%) and ulnar nerves (33%)as compared to controls.

Keywords: *Nerve conduction study, hypothyroidism, central India.*

Introduction

Thyroid gland has modulatory effect on the neuromuscular system and brain through its secretions, thyroxin (T4) and triiodothyronine (T3) which are essential to maintain metabolism in the tissues that is optimal for their normal growth,function and maturation[1].

Corresponding Author:
Dr. Ajay Meshram
Prof Dept Biochemistry, DMIMSU (DU) Sawangi, Wardha
e-mail: meshram.ajay66@gmail.com
Contact No.: 8308290768

Thyroid dysfunction is associated with characteristic symptoms and signs and functional alterations in many organs and systems. Central and peripheral nervous systems affection may provide the major presenting symptoms[2]. Prevalence of neuromuscular disorders related to thyroid dysfunction is 20-80 % [3].

Thyroid disease may cause signs and symptoms of neuromuscular dysfunction. Hypothyroidism has been associated with the clinical features of proximal muscle weakness; mononeuropathy and sensorimotor polyneuropathy [4]. Most of the patients of thyroid disorders with neuropathy are asymptomatic. The severity of the neuromuscular signs and symptoms are known to be related to the duration and degree of

hormonal deficiency[5]. Sometimes the nerve damage in untreated patients can lead to carpal tunnel syndrome and these patients end up getting hand surgery when they may have reversed that just by early screening with nerve conduction studies and getting treated for thyroid disorder[6].

The nerve conduction study (NCS) consists of Motor NCS, sensory NCS study. Motor nerve conduction studies assess motor axons by selectively recording muscle responses to nerve stimulation. In sensory nerve conduction studies SNAP is obtained by directly stimulating a sensory nerve and recording directly from it or its branches[7]. With a brief electrical pulse applied to the overlying skin, peripheral nerves can be easily stimulated and brought to an action potential [5]. Nerve conduction studies (NCV) are useful adjunct to the clinical examination of the peripheral nervous system. It is a test of the speed of signals through a nerve. They help to delineate the extent and distribution of the neural lesion and distinguish two major categories of peripheral nerve disease demyelination and axonal degeneration[6,8].

Complications occurring due to hypothyroidism are responsive to thyroid treatment or thyroid replacement therapy, but if are related to neuropathy then there could be a life long struggle with neuropathy pain if not treated promptly. Understanding neuropathy and hypothyroidism is crucial for all thyroid disease patients. Few studies are there who compare nerve conduction in early diagnosed hypothyroid disease with age and sex matched control group in rural population of central India. Electrophysiological studies are non invasive and helpful in early detection of neuropathy as they are most sensitive, specific and repeatable[9]. Neurological manifestations which may be noted in conjunction with systemic features of disease can be detected with nerve conduction studies[10,11]. Hence present study was conducted to assess the alterations of some selected variables of nerve conduction in early diagnosed hypothyroid patients and also to find out which type of neuropathy is more prevalent in those populations of rural area.

Aim: To assess the nerve conduction studies in the cases diagnosed as hypothyroidism.

Objectives:

1. To study the motor and sensory nerve conduction in the cases diagnosed as hypothyroidism.
2. To compare the motor and sensory nerve conduction of cases diagnosed as hypothyroidism with euthyroid subjects.
3. To evaluate type of neuropathy present in the cases diagnosed as hypothyroidism.

Method and Materials

Study Setting: Study was conducted at Central Neurophysiology laboratory in tertiary care teaching hospital, J.N.M.C, Sawangi (M), Wardha catering to rural population of central India.

Study Design: Cross-sectional comparative study.

Study Duration: Nine months

Sample Size:

Formula: $N = X^2.N.P\ (1\text{-}P)/C^2\ (N\text{-}1) + X^2.P\ (1\text{-}P)$

N = Total newly diagnosed patients

= 27

X^2 = Chi-square value for 1 degrees of freedom at some desired probability level is 3.84 at 5% level of significance.

P = 50% proportion

C = Confidence interval of one choice (95%)

= 0.05

$N = 3.84\times25\times0.5(0.5)/0.05^2\times49+3.84\times0.5\times0.5$

= 27

Study group -27 patient diagnosed as cases of hypothyroidism and

Control group -16 euthyroid subjects.

Inclusion Criteria:

- Study group included hypothyroid patients who were untreated of age 18-50 years[12] and both genders attending medicine outpatient department of AVBRH, Sawangi (M), Wardha.
- The diagnostic criteria for hypothyroidism were based on T_3, T_4 and TSH levels [4].
- Among the controls age and sex matched euthyroid subjects who had no past/present or family history of thyroid disorders and apparently healthy were included in the study.

Exclusion Criteria:

- Patients who were less than 18 years old to limit our study sample to the adult population.
- Patients suffering from secondary hypothyroidism or with other possible cause of neuropathy like diabetes mellitus, neuromuscular disorder, leprosy, drug induced neuropathy.
- Patients with family history of neuropathy, malignancy, HIV, liver and kidney diseases, myopathy, alcoholics, smokers and drug abuser were excluded from the study.

Methodology

After IEC clearance study was conducted in central physiology lab of AVBRH hospital, Sawangi (M) Wardha. Adult patients attending the outpatient department who were advised thyroid function tests were isolated and only those patients with biochemical evidence of hypothyroidism i.e. low tri – iodothyronine,thyroxine levels and thyroid stimulating hormone levels were enrolled for the study after getting their consent. Thyroid function tests were done in AVBRH hospital central lab by ADIVIA Centaur CP Immunoassay system of company Siemens (Photo-1). Normal values of lab were T3-0.60-1.81 ng/ml, T4-3.2-12.6 ug/ dl and TSH-0.25-5 µIU/ml. Patients were diagnosed cases of hypothyroidism who were not on any treatment, willing to participate in the study, were included in the study. Demographic parameters like height, weight and BMI were taken. Detailed history regarding neuromuscular symptoms with their duration based on questionnaire was asked. Age and gender matched healthy subjects with normal thyroid function tests were chosen as the control group for comparison.

Nerve conduction study was performed using the Neuron Spectrum 5 machine. The motor nerves tested were median, ulnar and peroneal. The sensory nerves studied were median,ulnar and sural. Parameters for motor nerve conduction study taken were latency (ms), amplitude (mv), conduction velocity (m/s) and for sensory nerve conduction study were amplitude (µv) and conduction velocity (m/s) [6]. Motor nerve conduction study involved stimulation of a motor nerve at two different sites with maximum stimulus, the distance was measured and automatically divided by conduction time between the two points (difference between proximal and distal motor latencies) which gave conduction velocity. Sensory conduction study (antidromic) involved stimulation of sensory nerves proximally and recording SNAPs with electrodes placed distally over the dermatomal distribution.

Result

Quantitative data analysis was done by using students unpaired' test and qualitative data by chi-square. All the values were expressed as mean and standard deviation (±SD) and p- value was considered statistically significant if found to be less than 0.05. GRAPHPAD PRISM 5.0 and SPSS 22.0 version was used.

Table 1: Distribution of patients according to demographic characteristics

Demographic Characteristics	Control (n = 16)	Hypothyroidism (n=27)	X^2 - Value	p-value
Mean Age	36.12±4.16	36.76±3.31	2.67	0.26,NS
18-30 yrs	0(0%)	2(7.41%)		
31-40 yrs	13(81.25%)	16(59.26%)		
41-50 yrs	3(18.75%)	9(33.33%)		
Gender				
Male	5(31.25%)	6(22.22%)	0.43	0.51,NS
Female	11(68.75%)	21(77.78%)		
M:F Ratio	1:2.2	1:2.5		
Wt (kg)	59.75±2.38	61.76±3.81	1.84	0.07,NS
Ht (cm)	155.50±5.54	154±5.75	0.79	0.43,NS

Demographic Characteristics	Control (n = 16)	Hypothyroidism (n=27)	X^2 - Value	p-value
BMI (kg/m2)	24.79±1.90	26.07±1.55	24.32	0.0001,S
Normal	16(100%)	6(22.22%)		
Overweight	0(0%)	9(33.33%)		
Obese	0(0%)	12(44.44%)		

Maximum 81.25% of the subjects in control group and 59.26% in hypothyroid group were in the age group of 31-40 years followed by 18.75% in control group and 33.33% in hypothyroid group were in the age group of 41-50 years which is statistically not significant using Chi-square test(א2-value=2.67,p-value=0.26).

Most of the subjects in control group (68.75%) and 77.78% in hypothyroid group were females which is statistically not significant (א2-value=0.43, p-value=0.51).

Mean weight of the subjects in control group was 59.75±2.38 and in hypothyroid group it was 61.76±3.81 and the difference was not significant using student's unpaired t test (t=1.84,p-value=0.07)

Mean height of the subjects in control group was 155.50±5.54 and in hypothyroid group it was 154±5.75and the difference was not significant using student's unpaired t test (t=0.79,p-value=0.43).

All(100%) of the subjects in control group had normal BMI, where as in hypothyroid group 44.44% of the patients were obese and 33.33% were overweight which is statistically significant א (א2-value=24.32, p-value=0.0001).

Table 2: Significant correlates of neuropathy

Demographic Characteristics	Abnormal Nerve Conduction(n=21)	Normal Nerve Conduction(n=6)	X^2- Value	p-value
18-30 yrs	1(4.76%)	1(16.67%)	1.00	0.60,NS
31-40 yrs	13(61.90%)	3(50%)		
41-50 yrs	7(33.33%)	2(33.33%)		
Gender				
Male	4(19.05%)	2(33.33%)	0.55	0.45,NS
Female	17(80.95%)	4(66.67%)		
Duration of disease				
<1 yr	6(28.57%)	3(50%)	0.96	0.61,NS
1-5 yrs	10(47.62%)	2(33.33%)		
>5 yrs	5(23.81%)	1(16.67%)		
BMI (kg/m^2)				
Normal	4(19.05%)	2(33.33%)	2.41	0.29,NS
Overweight	6(28.57%)	3(50%)		
Obese	11(52.38%)	1(16.67%)		
Signs and symptoms of neuropathy				
Absent	2(9.52%)	4(66.67%)	8.81	0.008,S
Present	19(90.48%)	2(33.33%)		

Maximum 61.90% of abnormal nerve conduction and 50% of normal nerve conduction was found in the age group of 31-40 years followed by 33.33% abnormal and 33.3% normal nerve conduction in the age group of 41-50 years,4.76% abnormal and 16.67 % normal nerve conduction in 18-20 years of age group in hypothyroid patients was observed which was statistically not significant (א2-value=1.00,p-value=0.60).

Most of the females 80.95% had abnormal nerve conduction while 66.67% had normal nerve conduction in hypothyroid group. Where as in males 19.05% had abnormal nerve conduction and 33.3% had normal nerve conduction which was statistically non significant (א2-value=0.55, p-value=0.45).

Maximum 47.62% of abnormal nerve conduction and 33.3% of normal nerve conduction was observed in 1-5 yrs duration, followed by 28.57% abnormal and 50% normal nerve conduction in less than one year,28.81% abnormal and 16.67 % normal nerve conduction in more than 5 years of duration of diseases in hypothyroid patients which was statistically not significant (א2-value=0.96,p-value=0.61).

Abnormal nerve conduction was observed maximum in obese hypothyroid patients 52.38% followed by 28.57% in overweight and 19.05% in normal weight hypothyroid group. Normal nerve conduction was found in 50% of overweight, 33.3% normal weight and 16.67% in obese hypothyroid patients which was not significant (א2-value=2.41, p-value=0.29).

Abnormal nerve conduction was present in 90.48% while 33.3% had normal nerve conduction in patients of hypothyroidism who showed signs and symptoms of neuropathy. Abnormal nerve conduction was present in 9.52% while 66.67% had normal nerve conduction in patients of hypothyroidism who didn't had signs and symptoms of neuropathy which was statistically significant (א2-value=8.81, p-value=0.008)

Discussion

Hypothyroidism is an endocrine disease and peripheral nervous system involvement is a well-documented. 20-80% of researchers have observed prevalence of neuromuscular disorders related to thyroid dysfunction, the severity of which correlates with the degree and duration of hormonal deficiency[3]. In fact neurological complications in hypothyroidism are a well-established finding. Peripheral nerve abnormalities known to be associated with hypothyroidism are entrapment neuropathy or sensorimotor polyneuropathy[13].

In hypothyroidism polyneuropathy is mild and rarely it could be a subclinical entity and hence most of these cases would have gone unnoticed if only clinical examination has been done as it alone may be insufficient to make a conclusive diagnosis specially to make a distinction between axonal and demyelinating disorders. At such times nerve conduction studies are particularly useful. They assess the functional integrity of sensorimotor conduction and give a reliable evidence of peripheral nerve dysfunction. In fact, the estimated prevalence of polyneuropathy diagnosed by electro physiologic tests is 718/1000 [(1).]

In our study on neurological examination two cases of hypothyroidism showed decreased reflexes. Out of 27 cases of diagnosed hypothyroidism 21 (77.78%) had at least one type of nerve conduction abnormality, most commonly in median and sural sensory nerves which was also observed in the studies done by Asia and Ettore et .al [(1,14)]. None of cases of hypothyroidism had signs of muscle atrophy or hypotonia. The commonly reported subjective complaints of tiredness, myalgias and weight gain were encountered in our study too. Tiredness, myalgias in 77.78%, weight gain in 59.26%, constipation in 37%, it correlates with other studies where it was 64% and 68% respectively [(14)]. Paresthesia were found in 33% and menstrual irregularities 22.2% was the next predominant symptoms. Similar results were also observed by Karne and Shetty et.al. [(8, 15)] The increased weight in cases of hypothyroidism would be due to accumulation of mucopolysaccharides, hyaluronic acid and chondroitin sulphate in the interstitial spaces. Those spaces being hydrophilic nature, retain water along with them resulting in weight gain. Also, hormonal imbalance leading to menstrual irregularities [(9)]. Neurological dysfunction associated with disorders of thyroid gland could be the result of hormonal imbalance or immune mechanism accompanying thyroid disease [(1)].

There are studies which reported primary axonal degeneration while some reported demyelination as the predominant feature of neuropathy in hypothyroidism[(8,15)]. In our study we got mixed type of peripheral neuropathy. SNAP amplitudes and Conduction velocity were significantly reduced($p<0.05$) in cases diagnosed as hypothyroidism as compared to controls in median (77%), sural (70%) and ulnar nerves (33%). Similar results were also observed by other studies [(14,15)].

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 nerve conduction changes in the form decreased nerve conduction velocity also thyroid hormones are involved in gene expression, neurotransmitter system and axonal transport , the plausible mechanism of axonal neuropathy is a hypothyroidism induced ATP deficiency with reduced activity of ATP ase enzyme may result in reduced SNAP amplitudes.

Similar to other researchers[9,13] distal latency and conduction velocity in our study was prolonged, amplitude was decreased in median motor nervesin early diagnosed hypothyroid patients as compared to that of control. This could be attributed to hypothyroidism leading to energy deficit due to decreased oxidation of nutrients also 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 [16].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.

Presence of neuropathy correlated independently with advanced age and female gender. Out of 27 patients with age 18-30 years 1 patient (16.67%), 31-40 years 13 patients (61.90%) and 41-50 years 7 patients (33.3%) showed abnormal nerve conduction. Occurrence of neuropathy was more common in female patients 80.95% as compared to male patients 19.05%. Similar results were also seen in studies conducted by other researchers[1,8,15]. Neuropathy was more common with duration of disease 1-5 years (47.62%) and obesity (52.38%) but these findings were not statistically significant (P = 0.60,0.45,0.61 and 0.29) respectively. Signs and symptoms of neuropathy was present in 19 patients (90.48%) of early diagnosed hypothyroid patients which was statistically significant (P = 0.008) as shown in Table 2.

Conclusion

This study concluded that the polyneuropathy which is associated with early diagnosed hypothyroidism was largely of mixed type (axonal as well as demyelinating type). There was a predominant involvement of sensory nerves, especially the median nerve and sural nerve on nerve conduction study. 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. Clinical symptoms and laboratory assessment of thyroid function must be performed concurrently to determine the presence of thyroid dysfunction. Nerve conduction studies in cases of hypothyroidism are suggested, early in the course of the disease in order to detect nervous system involvement.

Limitations: Major shortcomings of this study are the small sample size. Furthermore, we could not perform EMG in patients.

Risk Factor: As it is non- invasive study there was no harm to the study subjects.

Ethical Clearance: Taken from institutional ethics committee.

Source of Funding: Self.

Conflict of Interest: Nil.

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