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Carpal tunnel syndrome in hypothyroid patients: The effect of hormone replacement therapy

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Abstract: Objectives: To assess the electrodiagnostic evidence of median nerve dysfunction in newly diagnosed hypothyroid patients before and after hormone replacement therapy. Patients and methods: Fifty seven patients (fifty females and seven males) their age ranging from 23 to 61 years diagnosed with hypothyroidism,proved by thyroid hormone profile,were included in this study. Electrodiagnostic workup performed at the initial time of diagnosis and after 3 months including motor and sensory median nerve conduction studies in both right and left median nerves. Results: In our studied group, TSH levels were 30.77±23.51 IU/ mL before hormone replacement therapy and 5.25±1.72 IU/mL after the treatment. FT4 values were 9.2±1.54 pmol/l before treatment and 15.42±2.62pmol/l after treatment. FT3 levels were measured as 1.69±0.63Pmol/l at the diagnosis and 4.23±1.04 Pmol/l after treatment. The pre and post therapy levels difference of all previous parameters were statistically significant(P =0.001). Forty eight patients were normalized after treatment, while nine (13.8%) still had carpal tunnel syndrome symptoms. The differences between before treatment values of median nerve sensory and motor functions in both right and left median nerves respectively (sensory distal latency, sensory nerve conduction velocity, the sensory amplitude, the motor distal latency, the motor conduction velocity and the motor amplitude)(4.156±0.49 and 14.789±8.36 , 51.730±2.32 and 52.088±2.42, 28.123±8.52 and 25.193±5.74 , 4.404±0.66 and 4.393±0.61, 53.074±3.38 and 52.867±3.82 , 4.830±1.09 and 4.984±1.29) and after treatment values (3.365±0.44 and 3.561±0.46 , 63.649±2.16 and 63.035±3.56 , 33.123±7.16 and 29.280±5.39 , 3.674±0.52 and 3.767±0.46 , 64.193±2.79 and 63.789±4.00 , 5.368±1.18 and 5.488±1.19) were all significant (P =0.001). Conclusion: With hormonal replacement therapy, carpal tunnel syndrome can be reserved in patients with hypothyroidism within three months.

Keywords: Carpal Tunnel Syndrome, Hypothyroidism, Median Nerve

1. Introduction

Thyroid hormones are involved in many functions of the central and peripheral nervous system and as a result, hypothyroidism may cause various neurological signs and symptoms (1, 7,17, 27).

Hypothyroidism is a clinical condition associated with low levels of thyroid hormones with raised thyroid stimulating hormone (TSH). It may be due to some intrinsic disorders in thyroid or may be disorder in pituitary or hypothalamus (13, 26).

The investigators studied nerve conduction parameters in hypothyroid patients to observe the incidence of neuropathy and functional status of peripheral nerves in thyroid deficiency. Most of them had shown that deficiency of thyroid hormones cause motor neuropathy by affecting different peripheral nerves but more commonly the median nerve (26).

Earlier retrospective studies reported the prevalence of neuropathy to be 10–70% in patients with hypothyroidism . The most common entrapment neuropathy is the carpal tunnel syndrome (CTS) , which results of an increased pressure on the median nerve at the wrist, due to the accumulation of amynoglycane matter (16,17).

The pathogenesis of peripheral nerve abnormalities in thyroid dysfunction is still unclear. A mononeuropathy

secondary to compression caused by mucinous deposits in the soft tissues surrounding peripheral nerves and a polyneuropathy due to either a demyelinating process or primary axonal degeneration have been proposed in etiology (2).

Previous studies have demonstrated that structural alterations of myelin and dysfunction of axonal-oligodendroglial processes are responsible for neuropathy in patients with hypothyroidism (6,12).

Also, hypothyroidism produces alterations of fluid balance and peripheral tissue edema, which may lead to CTS development (3,4). Consequently, treatment of hypothyroidism, may help to reduce or cure CTS complaints (9) (10) .

In our study, we are aiming to document median nerve entrapment in patients with hypothyroidism and to assess the changes in electrodiagnostic findings before and after hormone replacement therapy.

2. Patients and Methods

2.1. Patients

Patients with hypothyroidism were recruited from the internal medicine, surgery outpatient department of our faculties hospital. Between April 2011 and July 2011 , 57 consecutive patients above 18 years were recruited, irrespective of whether they had neurological complaints or not. As they were newly diagnosed, none of these patients received any medical treatment for hypothyroidism or its complications. All patients were informed about the content of the study and gave their written approvals before enrollment. Laboratory investigations including complete blood count, serum glucose, creatinine, electrolytes, liver and kidney enzymes, vitamin B12 and folic acid tests were performed at the onset of the study in order to eliminate other possible causes of neuropathy. Patients showing other causes of neuropathy such as diabetes mellitus, alcoholism, liver and kidney disease, use of drugs known to cause neuropathy, malignancy or other serious illness and patients with a family history of neuropathy were excluded from the study. Serum analyses were performed to confirm the hypothyroid state, after a detailed neurological examination. For this, free T3, free T4 and TSH levels were evaluated. Reference values for our laboratory for TSH were between 0.27 and 4.2 IU/ml, for FT4 between 11.6 and 22 pmol/l, and for FT3 between 2.8 and 7.1 pmol/l. Patients with FT4 levels below 11.6 pmol/ml and TSH levels above 4.2 IU/ml were accepted as hypothyroidism and underwent the initial electrodiagnostic evaluation according to standard techniques.Only 57 patients proned to have carpal tunnel syndrome included in our study. Thereafter, all patients received appropriate doses of thyroxin treatment for hypothyroidism and were monthly followed up for FT4, FT3 and TSH levels throughout a 3 month period. At the end of this period, patients with biochemical euthyroidism underwent control electrodiagnostic evaluation.

2.2. Electrodiagnostic Evaluation

The electrodiagnostic studies were performed according to standard techniques (11). These were performed in at least two arms and one leg. Motor nerve conduction studies included the determination of conduction velocity, amplitudes and latencies after stimulation of the median nerve. Sensory nerve conduction studies included the antidromic determination of conduction velocity, latencies and amplitude of the sensory nerve action potential of the median nerve. A carpal tunnel syndrome was diagnosed when the median nerve distal motor and/or sensory latencies exceeded 4.4 and 3.5 ms, respectively (12). Distance between stimulation site and active electrode was 14 cm for median nerve sensory study.

Statistical analyses were performed using SPSS version 16, all tests done by the student t- test and were values expressed as mean ± SD.

3. Results

Fifty seven patients with hypothyroidism and with electrodiagnostic evidences of carpal tunnel syndrome were subjected to hormone replacement therapy and reevaluated by biochemical and electrophysiological studies. Among our patients (50 women and 7 men , the mean age was 42.7 ±12.1 (23-61) years. All are newly diagnosed as hypothyroidism. TSH levels were 30.77±23.51 IU/mL before hormone replacement therapy and 5.25±1.72 IU/mL after the treatment. This difference was statistically significant (t= 8.609, P 0.001). FT4 values were 9.2±1.54 pmol/l before treatment and 15.42±2.62pmol/l after treatment; this was statistically significant (t= 19.837, P value 0.001). FT3 levels were measured as 1.69± 0.63Pmol/l at the diagnosis and 4.23±1.04 Pmol/l after treatment. This was also statistically significant (t= 16.602, P 0.001).

At the initial time of assessment, all patients had electrodiagnostic evidence of carpal tunnel syndrome. The sensory conduction parameters in our patients revealed that the sensory distal latency before Hormonal replacement therapy(HRT) was high in both right and left median nerves 4.156±0.49 and 14.789±8.36 respectively and these levels were significantly decreased after Hormonal replacement therapy to 3.365±0.44 and 3.561±0.46 (P<0.001). The sensory nerve conduction velocity in our patients before HRT was low in both right and left median nerves 51.730±2.32 and 52.088±2.42 respectively and the levels were significantly increased to 63.649±2.16 and 63.035±3.56 after HRT (P<0.001).The sensory amplitude in our patients before HRT was low in right and left median nerves 28.123±8.52 and 25.193±5.74 respectively, and significantly increased after HRT to 33.123±7.16 and 29.280±5.39 (P<0.001) Table 2. As regard to motor conduction parameters, the motor distal latency was high in in right and left median nerves before HRT 4.404±0.66 and 4.393±0.61 respectively and significantly decreased after HRT to 3.674±0.52 and 3.767±0.46 (P<0.001). The motor

conduction velocity was lower in right and left median nerves before HRT 53.074±3.38 and 52.867±3.82 respectively and significantly increased after HRT to 64.193±2.79 and 63.789±4.00 (P<0.001) and lastly, the motor amplitude in our patients was low before HRT in right and left median nerves 4.830±1.09 and 4.984±1.29 respectively and significantly increased after HRT to 5.368±1.18 and 5.488±1.19 (P<0.001) Table 3. After 3 months of appropriate hormonal replacement therapy, only nine patients(13.8%) still had manifestations of carpal tunnel syndrome and sended back to the general surgeon for surgical decompression.

Table 1. *TSH, FT4, and FT3 before and after Hormone replacement therapy (HRT).*

		Range	M+ SD	t	P
TSH	Before HRT	6.5 - 100	30.76 + 32.52	8.609	< 0.001
	After HRT	2.8 – 9.1	5.251+ 1.72		
FT4	Before HRT	6.2 - 14	9.198+ 1.54	19.837	< 0.001
	After HRT	10.8-20	15.418+ 2.62		
FT3	Before HRT	0.8 - 3	1.695+ 0.63	16.602	<0.001
	After HRT	2.8 – 6.8	4.226+ 1.04		

Table 2. *Sensory conduction parameters of the tested median nerves in our patients before and after Hormone replacement therapy(HRT).*

Parameters	Before HRT (Mean±SD)	After HRT (Mean±SD)	t	P
Rt Med. N. Sensory distal latency(m/sec)	4.156±0.49	3.365±0.44	13.19	<0.001
Lt Med. N. Sensory distal latency(m/sec)	14.789±8.36	3.561±0.46	10.17	<0.001
Rt. Med. N. Sensory Nerve Conduction Velocity(NCV) (m/sec)	51.730±2.32	63.649±2.16	11.31	<0.001
Lt. Med. N. Sensory NCV (m/sec)	52.088±2.42	63.035±3.56	6.41	<0.001
Rt. Med. N. Sensory Amplitude(m. volt)	28.123±8.52	33.123±7.16	3.93	<0.001
Lt. Med. N. Sensory Amplitude(m. volt)	25.193±5.74	29.280±5.39	7.53	<0.001

Table 3. *Motor conduction parameters of the tested median nerves in our patients before and after HRT.*

Parameters	Before HRT	After HRT	t	P
Rt. Med.N. Motor distal latency(m/sec)	4.404±0.66	3.674±0.52	10.37	<0.001
Lt .Med. N. Motor distal latency(m/sec)	4.393±0.61	3.767±0.46	10.15	<0.001
Rt. Med. N. Motor NCV(m/sec)	53.074±3.38	64.193±2.79	4.08	<0.001
Lt. Med. N. Motor NCV(m/sec)	52.867±3.82	63.789±4.00	5.66	<0.001
Rt. Med. N. Motor amplitude (µ. Volt)	4.830±1.09	5.368±1.18	5.97	<0.001
Lt. Med. N Motor amplitude (µ. Volt)	4.984±1.29	5.488±1.19	6.45	<0.001

4. Discussion

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. 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, parasthesia 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 (14, 24, 27).

The mechanism involved in the development of neuropathy in hypothyroidism still remains unclear (22,24). Mononeuropathies secondary to compression caused by deposition of mucopolysaccharide or mucinous deposits in the soft tissues surrounding peripheral nerves and a polyneuropathy due to either a demyelinating process or primary axonal degeneration are the most commonly proposed mechanisms of peripheral nerve dysfunction in hypothyroidism (16,20). Myelin structure abnormalities and dysfunction of axonal-oligodendroglial processes may also be responsible for neuropathy in patients with hypothyroidism (10,15).

In this study, all hypothyroid patients had significantly higher TSH levels and significantly lower FT4 and FT3 levels before the hormone replacement therapy. Also, a significant number of our patients showed nerve conduction

abnormalities. At the initial time of assessement, all patients had electrodiagnostic evidence of carpal tunnel syndrome.

In our patients, there were higher sensory and motor distal latencies with lower both motor, sensory nerve conduction velocities and lower motor and sensory median nerve amplitude. These correlates with some groups of investigators of different countries that revealed similar involvement of the motor portion of the median nerve and slowing of the nerve conduction velocities in different peripheral nerves but they did not mention about the individual values of the parameters like sensory distal latencies and sensory nerve conduction velocities (16, 17, 19).

One earlier study reported that 52% of hypothyroid patients with peripheral nervous system involvement, entrapment neuropathy was the commonest(35%) and axonal neuropathy was recorded in 9% of these patients(17).

In our study, all patients had electrophysiological evidence of carpal tunnel syndrome thus, hypothyroidism is considered a risk factor for carpal tunnel syndrome but the nature of this association is still obscure(24). Most previous studies revealed that despite obtaining an euthyroid state, most patients with diagnosis of primary hypothyroidism continue to experience symptoms and electrophysiological signs of carpal tunnel syndrome(2, 18).

In this study, all patients are newly diagnosed with hypothyroidism and the carpal tunnel syndrome symptoms improve their thyroid functions after hormonal replacement therapy. The TSH levels before treatment was 30.77±23.51 IU/Ml and the levels were changed to 5.25±1.72IU/Ml after hormonal replacement therapy (p 0.001). The FT4 and FT3 levels were significantly increased after treatment (p 0.001) and these correlates with study done by Kececi and Degirmenci 2006.

In our study, only nine patients(13.8%) still had carpal tunnel syndrome manifestations after replacement therapy and subjected to surgical decompression. This suggests that the mechanism leading to carpal tunnel syndrome in patients with hypothyroidism might be reversible at early stages; on the other hand irreversible cases might have longer duration of disease or might present etiologies other than hypothyroid. Long term accumulation of mucinous tissue is a possible cause of irreversibility (16).

A limited number of studies suggest that polyneuropathy would be the initial and predominant finding especially in newly diagnosed hypothyroid cases (7, 20,23). The majority of our patients with a diagnosis of polyneuropathy had electrophysiological evidence of prominent sensory neuropathy involving the median nerve. Among these, 86.2% showed improvement after hormone replacement therapy while 13.8% still showed evidence of sensory neuropathy. The cause of irreversibility to replacement therapy in these patients may be related to differences in illness durations, severity and treatment regimens (5,14, 17, 21,24).

The majority of earlier studies (2,7,9, 21,23,24) in patients with primary or subclinical hypothyroidism only included electrophysiological evaluation before treatment. In our study, we performed a comparison study after appropriate dosages of hormone replacement therapy. This additional evaluation gives the opportunity to evaluate the efficacy of replacement therapy on the peripheral nerve disturbance either motor or sensory neuropathy. The follow up of our patients after treatment demonstrate that the abnormalities related to entrapment neuropathy and polyneuropathy in hypothyroid patients can be reversed within three months of hormonal replacement therapy.

In conclusion, in the presence of entrapment neuropathy in hypothyroidism the chance of appropriate hormone replacement treatment must be given to newly diagnosed patients before considering surgical decompression treatment.

References

[1] Allessio P, Alessandro S, Elena A, Giovanni M, Michele C, Carlo D, Andrea M. Morphologic and functional evaluation of the carpal tunnel syndrome before and after treatment. 116(1) (supplement) 2011.

[2] Arikan E, Pekindil G, Guldiken S, Pekindil Y. Evaluation of median nerve in subclinical hypothyroidism by high-resolution sonography. Turkish Journal of Endocrinology and Metabolism, 2005, (1) : 63-67.

[3] Beghni E, Deledovici M, Boglium G, Crespi V, Paleari F, Gamba P, Capra M, Zarrelli. Hypothyroidism and polyneuropathy. J Neurol Neurosurg. Psychiatry; 52: 1420-1423, 1989.

[4] Dawson DM. Entrapment neuropathies of the upper extrimities. N Engl J Med. 1993; 329 :(2013).

[5] Deniz Y, Eda E, Filiz K. The effects of hypothyroidism on strength-duration properties of peripheral nerve. J. Neurological Sciences 294(1-2): 89-91. 2010.

[6] Dijk MAJ, Reitsma JB, Fischer JC, Sanders GTB. Indications for requesting laboratory tests for concurrent diseases in patients with carpal tunnel syndrome. A systematic review. Clinical Chemistry 2003, 49(9): 1437-1444.

[7] Duffy RF, Van den Bosch J, Laman DM, van Loon BJB, Linssen WHJP. Neuromuscular findings in thyroid dysfunction: a prospective clinical and electrodiagnostic study. J. Neurol. Neurosurg. Psychiatry 2000, 68: 750-755.

[8] El-salem K, Ammari F. Neurophysiological changes in neurologically A symptomatic Hypothyroid patients: A prospective cohort study.Journal Clinical Neurophysiology. 23(6): 568-572.

[9] Eslamin F, Bahrami A, Niafar M, Salehzamani Y, Behkamrad K. Electrophysiologic changes in patients with untreated primary hypothyroidism. J. Clinical Neurophysiol 28(3): 323-328. 2011.

[10] Ferracci F, Carnevale A. The neurological disorder associated with thyroid autoimmunity. J. Neurol. 2006; 253(8): 975-984.

[11] Ferreira AA, Nazario JC, Periera PJ, Azevedo NL, Barradas PC. Effects of experimental hypothyroidism on myelin sheath structural organization. J. Neurocytol.2004; 33(2): 225-231.

[12] Galea LA, Gatt R, Sciberras C: Hand and wrist configurations in patients with carpal tunnel syndrome. Malta Medical Journal 2007; 19(02): 32-34.

[13] Ganong WF. The thyroid gland. In: Review of medical physiology 21 Edition. MC Graw Hill, Boston 2003, pp 320-335.

[14] Giuseppel And Grazia D. Skin biopsy as a diagnostic tool in peripheral neuropathy. Nature Clinical Practice Neurology.2oo7; 3(10): 546-557.

[15] Jameson JL, Wretman AP. Disorders of thyroid gland. In: Braunwald E, Fauci AS, Kasper DL, Editors. Harrison's Principles of Internal Medicine, 15th ed. Mc Graw-Hill; 2001: 2060-84.

[16] Kececi H, Degirmenci Y. Hormone replacement therapy in hypothyroidism and nerve conduction study. Clinical Neurophysiology; 2006; 36: 79-83.

[17] Khedr EM, El-toony LF, Tarkhan MN, Abdalla G. Peripheral and central nervous system alterations in hypothyroidism: Electrophysiological findings. Neuropsychobiology., 41(2): 88-94; 2000.

[18] Kimura G. Assesment of individual nerves. Electrodiagnosis in diseases of nerve and muscle: Principles and practice Edition 3. New York: Oxford University Press; 2001: 130-77.

[19] Nebuchennykh M, Loseth S, Mellegren S. Aspects of peripheral nerve involvement in patients with treated hypothyroidism. European Journal of Neurology, issue1, pages 67-72, 2010.

[20] Nemni R, Bottachi E, Fazio R. Polyneuropathy in hypothyroidism: clinical, electrophysiological and morphological finding in our cases.J Neurol Neurosurg Psychiatry 1987; 50: 1454-60.

[21] Preston DC, Shapiro BE. Electromyography and neuromuscular disorders, 2nd edition. Appendix; Butterworth- Heinemann; 2005: 561-4.

[22] Rao SN, Katiyar BC, Nair KR, Misra S. Neuromuscular status in hypothyroidism. Acta Neurol Scand 1980; 61 : 167-77.

[23] Sabina Y, Noorzadah B, Shelina B. Motor neuropathy in hypothyroidism: clinical and electrophysiological findings. BSMMU J. 2008; 1(1): 15-18.

[24] Shirabe T, Tawara S, Terao A, Araki S. Myxedematous poly neuropathy. A light and electron microscopy study of the peripheral nerve and muscle. J. Neurol. Neurosurg. Psychiatry 1975; 38: 241-7.

[25] Somay G, Oflazoglo B, Us O, Surandamar A. Neuromuscular status of thyroid diseases, a prospective clinical and electrodiagnostic study. Electromyogr. Clin. Neurophysiol. 2007; 47(2): 67-78.

[26] Yeasmin S,Begum S, Rahman SMH. Sensory neuropathy in hypothyroidism: Electrophysiological and clinical findings. Journal Of Bangladish Society Of Physiologist, Volume 2, 2007: 1-6.

[27] Yuksel G, Karlikaya G, Tanridag T, Us O, Akyuz G. Nerve conduction studies, SEP and Blink reflex studies in recently diagnosed, untreated thyroid disease patients. J. Neurol. Sci.[Turk] 2007; 24:7-15.