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Original Article / Özgün Araştırma

Electromyographic Findings in Overt Hypothyroidism and Subclinical Hypothyroidism

Aşikar Hipotiroidizm ve Subklinik Hipotiroidizmde Elektromiyografik Bulgular

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Summary

Objective: Hypothyroidism may cause neurologic signs and symptoms as it affects neuromuscular system in addition to many other systems. Subclinical hypothyroidism is the most common form of thyroid dysfunction and it may cause neuromuscular symptoms. In this retrospective study, we aimed to compare hypothyroid patients and healthy controls with normal thyroid function and without a disease-causing polyneuropathy, in terms of their neuromuscular symptoms and electromyographic (EMG) findings.

Methods: The patient group consisted of 31 overt hypothyroidic, 139 subclinic hypothyroidic patients and healthy control group consisted of 50 individuals with normal thyroid function and without a disease causing polyneuropathy, whom had EMG records for other reasons were included in the study. Neuromuscular symptoms, and neurological examination and electrophysiological findings were obtained from the patient records.

Results: In our study, we observed frequent neuromuscular complaints such as fatigue, morning stiffness, cramp, general pain and paresthesia in both overt and subclinic hypothyroidism patients. Carpal tunnel syndrome (CTS), was statistically higher in overt hypothyroidism group than in control group. Carpal tunnel syndrome was also observed more frequently in subclinic hypothyroidism group compared to control group but the difference did not reach statistical significance. We did not detect polyneuropathy in any group. The differences in motor nerve velocity and compound muscle action potential amplitudes were found to be statistically significant between hypothyroid and control group.

Conclusion: Involvement of motor fibers and neuromuscular areas in hypothyroidism due to reduced basal metabolism activity can show significant recovery following thyroid replacement therapy. We believe in the need for future studies comparing pre-treatment electrophysiological findings to post-treatment findings. *(Turkish Journal of Neurology 2013; 19: 128-133)*

Key Words: Hypothyroidism, neurologic signs and symptoms, electromyography

Özet

Amaç: Hipotiroidizm, bir çok sistem gibi nöromuskuler sistemi de etkileyerek nörolojik belirti ve semptomlara yol açar. Subklinik hipotiroidizm en sık görülen tiroid fonksiyon bozukluğudur ve nörolojik semptomlara yol açabilir. Bu retrospektif çalışmada, hipotiroidisi olan hastalar ile tiroid fonksiyonları normal olan, polinöropatiye yol açacak hastalığı olmayan kontrol grubunun, nörolojik semptomlar ve elektromiyografik (EMG) bulgular açısından karşılaştırılması amaçlandı.

Gereç ve Yöntem: Çalışmaya 31 aşikar hipotiroidili, 139 subklinik hipotiroidili hasta ve 50 normal tiroid fonksiyonlu olup başka bir polinöropati yapabilecek hastalığı olmayan, herhangi bir nedenle EMG incelemesi yapılmış olan bireyler dahil edildi. Nörolojik semptom, muayene ve elektrofizyolojik bulgulara hasta kayıtlarından ulaşıldı.

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Bulgular: Çalışmamızda aşikar ve subklinik hipotiroidi grubunda yorgunluk, sabah katılığı, kramp, genel ağrı ve parestezi gibi nöromuskuler şikayetlerin sıklıkla var olduğu gözlendi. Karpal tünel sendromu (KTS), aşikar hipotiroidi grubunda kontrol grubuna göre istatistiksel olarak anlamlı yüksek saptandı. Karpal tünel sendromunun subklinik hipotiroidi grubunda da kontrollere göre daha sık olduğu, ancak istatistiksel anlamlılığa ulaşmadığı gözlendi. Motor ileti hızı ve bileşik kas aksiyon potansiyeli amplitüdlerinde kontrol grubu ile hipotiroidi grupları arasında farklılık olduğu saptandı.

Sonuç: Hipotiroidizmde motor liflerin ve nöromusküler bölgenin bazal metabolizmanın yavaşlamasına bağlı olduğunu düşündüğümüz etkilenmeleri, tiroid replasman tedavisi sonrası belirgin düzelme gösterebilir. İleriki çalışmalarda tedavi sonrası elektrofizyolojik bulguların tedavi öncesi bulgular ile karşılaştırılmasının yapılması gerektiğini düşünmekteyiz. *(Türk Nöroloji Dergisi 2013; 19:128-133)*

Anahtar Kelimeler: Hipotiroidizm, nörolojik semptomlar, elektromiyografi

Introduction

Hypothyroidism causes neurological symptoms by involving the neuromuscular system in addition to many others. Studies showed neuropathy or myopathy symptoms with a rate of 80% in hypothyroidism (1). There is electrophysiological evidence showing the most common neuropathy in hypothyroidism is the carpal tunnel syndrome (CTS) (2,3).

Subclinical hypothyroidism's effect on the peripheral nerves and muscles has been a matter of debate. There has been evidence suggesting the existence of neuromuscular symptoms and signs in also subclinical hypothyroidism (4,5). Some studies, however, did not report any peripheral nerve involvement (6,7).

In this retrospective study, we investigated the frequency of neuropathy and myopathy in patients diagnosed with overt and subclinical hypothyroidism by using their laboratory and electromyography (EMG) results. Based on clinical, laboratory and EMG data, these two hypothyroid groups were compared to a control group consisted of patients who underwent EMG examination for other reasons, and who had normal thyroid functions without any other conditions associated with polyneuropathy (PNP).

Materials and Methods

Local ethics committee approved the methods of the study which uses archival data from electrophysiology laboratory between the years 2009-2011. The study included 200 individuals who consulted in our hospital's polyclinic and were evaluated in the electrophysiology lab. Thirty one patients with overt hypothyroidism (group 1: 29 female, 2 male), 119 patients with subclinical hypothyroidism (group 2: 106 female, 13 male) were included in the study. Fifty patients with normal thyroid functioning (group 3: 45 female, 5 male) were included in the study as the control group.

Patients with chronic diseases (diabetes mellitus, chronic liver or chronic kidney diseases, chronic infection, anemia), history of toxin exposure, hereditary neuropathy or myopathy, alcohol or substance dependencies or those who showed high pre-meal blood glucose levels, vitamin B12 deficiencies, abnormal liver function results and high urea-creatinine in laboratory tests were excluded from the study.

Medical history of all patients in the study included symptoms indicative of neuropathy or myopathy such as fatigue, paresthesia, wide-spread pain and cramps. The reported symptoms, neurological examination notes, creatine kinase (CK) levels, nerve conduction tests and needle EMG results were reviewed from each patient's records.

The EMG data acquired following the standard protocols was evaluated. In the motor conduction velocity (MCV) evaluations, median, ulnar, peroneal and tibial nerves MCVs, distal latencies (DL) and compound muscle action potentials (CMAP); in the sensory conduction velocity evaluations (SCV), DL and sensory action potentials (SAP) were investigated. Reference values and their deviations following standard procedures were derived from the literature. Among the nerves studied electrophysiologically, if one or more of them was affected, and if the nature of this involvement was in line with a pathological character (SAP amplitude reduction, SCV slowness, motor DL increase, CMAP amplitude reduction, MCV slowness), the case was determined to have PNP (8).

Motor unit potentials (MUP) recorded using concentric needle electrodes were analyzed using their amplitudes, durations and phases.

Results

SPSS for Windows 10.0 was used in the data analysis. For the comparisons Student's t-test, Mann-Whitney U, chi-square, ANOVA and Kruskal-Wallis tests were used. Statistical significance threshold was determined as $p<0.05$.

The age and sex distribution of the groups are summarized in Table 1. Overt hypothyroid group was found to have significantly higher CK level compared to other groups (Table 1).

The most commonly seen symptoms in our overt hypothyroidism group were fatigue with a rate of 64.5%, paresthesia with 58%, wide-spread pain with 58% and cramps with 38.7%. In the subclinical group the symptoms were fatigue with 49.58%, paresthesis with 31.09%, 31% wide-spread pain, and cramps with 21.01%. When subclinical hypothyroid and overt hypothyroid symptoms were compared to control groups, the symptoms were seen to be more frequent in the hypothyroid groups (Table 2).

Two of the patients in the overt hypothyroidism group had proximal dominant tetraparesis. Even though other patients and the control group had symptoms for neuropathy and myopathy, their neurological examination did not reveal muscle weakness, diminished deep tendon reflex or glove-stocking type sensory deficits that would suggest myopathy or PNP.

In our study, we found CTS in 13 patients out of 31 overt hypothyroid patients (41.9%), 25 out of 119 subclinical hypothyroid patients (21%). In the control group, 6 patients out of 50 (12%) had CTS. When the incidence rate of CTS in overt hypothyroid group was compared to other two groups, it was found to be higher than both the subclinical hypothyroid ($p<0.01$) and the control groups ($p<0.02$). The incidence rate of CTS was qualitatively higher in the

subclinical hypothyroid group than the control group, even though this difference did not reach statistical significance. Twelve (92.3%) of the 13 patients with CTS in overt hypothyroid group, 22 (88%) of the 25 patients with CTS in the subclinical hypothyroid group and 4 (66%) of the 6 patients with CTS was bilateral.

None of the patients included in the study had PNP. Two patients in the overt hypothyroid group had myopathy. Incidence rates for PNP, entrapment neuropathy and myopathies in the patient groups and the control group are show in Table 3.

An electrophysiological comparison of the patient groups with the control group is shown in the Table 4.

Discussion

Our study replicated the findings in the literature suggesting that there is a higher frequency for cramps (1,9-11), complaints of fatigue by 40-70% (1, 4, 12), wide-spread pain (4,10,13,14) and paresthesia (5,15) in hypothyroidism. Even though subclinical hypothyroidism is theoretically asymptomatic, our study showed an increase in neuromuscular symptoms in accordance with the literature.

An overall slowness in all metabolic pathways is seen in hypothyroidism. Due to the reduction of the carbohydrate metabolism, glycosaminoglycans cannot be broken down and instead accumulate in the entrapment regions leading to entrapment neuropathies (15,16). Moreover, the disruption of cellular respiratory cycle leads to a decreased rate of ATP synthesis, dysfunction of the Na-K pump and consequently an axonal transport disruption, which increases the susceptibility of the entrapment regions (17). It is hypothesized that CTS in hypothyroidism develops as a result of the mucinosis infiltration in the median nerve perineurium and

Table 1. Summary of group properties and demographics

	Overt hypothyroidism (n=31)	Subclinical hypothyroidism (n=139)	Control (n=50)	P
F/M	29/2	106/13	45/5	0.761
Mean age	45.65±12.55	40.07±13.69	40.38±9.27	0.075
TSH (mIU/ml) level	38.56±40.54	8.48±5.35	1.83±0.93	0.001*
fT4 (pg/ml)	0.59±0.14	1.05±0.20	1.12±0.20	0.001*
fT3 (pg/ml)	2.17±0.75	2.72±0.69	2.73±0.40	0.001*
CK (U/l)	81.50±43.55	232.55±413.72	83.37±36.46	0.001*

*: p<0.05, TSH: Thyroid stimulating hormone, fT4: free T4, fT3:free T3, CK: Creatine kinase

Table 2. A comparison of complaints in different study group

	Overt hypothyroidism (1)	Subclinical hypothyroidism (2)	Control (3)	P (1-3)	P (2-3)	P (1-2)
Fatigue	%64.5	%49.5	%30	0.003*	0.027*	0.161
Morning stiffness	%41	%30.2	%10	0.002*	0.005*	0.282
Cramp	%38.7	%21	%8	0.001*	0.045*	0.060
Wide-spread pain	%58	%31	%16	0.001*	0.056	0.007*
Paresthesia	%58	%31.009	%18	0.010*	0.091	0.007*

* : p<0,05

Table 3. The ratio of entrapment neuropathy, polyneuropathy and myopathy ratios in study groups

	Overt hypothyroidism (n=31)	Subclinical hypothyroidism (n=139)	Control (3) (n=50)	P (1-3)	P (2-3)	P (1-2)
Carpal tunnel syndrome (one side/both sides)	1/12	3/22	2/4	0.003*	0.197	0.022*
Ulnar neuropathy on ulnar segment	1	1	0	0.383	0.516	0.128
Polyneuropathy	0	0	0			
Myopathy	2	0	0	0.144		0.042*

* : p<0,05

Table 4. Comparison of electrophysiological results of study groups

	Overt hypothyroid (1)	Subclincal hypothyroid (2)	Control (3)	P (1-3)	P(2-3)
Conduction velocity (m/s)					
Median motor	56.26±5.24	59.87±5.04	61.16±4.30	0.001*	0.08
Median sensory	51.18±8.33	54.27±8.13	54.72±6.12	0.035*	0.469
Ulnar motor	62.33±5.91	62.94±5.78	65.85±6.55	0.017*	0.009*
Ulnar sensory	55.72±5.39	55.77±4.72	56.29±5.74	0.865	0.909
Tibial motor	46.95±4.72	47.76±4.84	48.92±5.57	0.193	0.31
Peroneal motor	47.39±4.76	49.62±4.49	53.15±9.69	0.001*	0.001*
Sural sensory	52.54±7.99	53.27±5.90	53.06±5.01	0.321	0.982
Latans (ms)					
Median motor	3.61±0.62	3.10±0.60	3.10±0.42	0.001*	0.198
Ulnar motor	2.53±0.46	2.35±0.34	2.42±0.35	0.459	0.081
Peroneal motor	4.10±1.12	3.79±0.62	3.92±0.58	0.076	0.136
Tibial motor	4.52±0.96	4.17±0.81	4.14±0.79	0.071	0.655
Amplitüde (mV)					
Median motor	8.77±2.43	9.99±2.41	9.79±2.73	0.022*	0.593
Median sensory	19.46±10.79	24.11±9.97	23.40±11.86	0.16	0.366
Ulnar motor	10.02±1.87	10.67±1.72	10.66±1.72	0.185	0.843
Ulnar sensory	14.69±5.99	16.63±5.87	15.17±5.01	0.331	0.171
Tibial motor	7.01±2.00	8.28±2.73	8.49±2.94	0.027*	0.844
Peroneal motor	2.74±0.87	3.57±1.52	4.72±1.68	0.001*	0.001*
Sural sensory	15.03±3.47	16.48±6.01	15.87±4.58	0.547	0.805

*: p<0,05

endoneurium. The increased pressure as a result of this infiltration is transferred to the median nerve and causes focal demyelination (18). Considering the fact that thyroid functions decreased in subclinical hypothyroidism, it is easy to expect these symptoms in subclinical cases although possibly to a lesser extent than the overt hypothyroidism. There are different reports in the literature about the co-occurrence of hypothyroidism with CTS. Suresh et al. (19) reported only a mild increase in CTS rate due to thyroid dysfunctions (hypothyroidism or hyperthyroidism). van Dijk et al.'s (20) review estimated the prevalence of hypothyroidism in people with CTS between 1.3% and 10.3%. Rijk et al. (21) reported a rate of 12.5% for CTS in subclinical hypothyroid cases. In some other studies, on the other hand, reports have been as high as 25-40% (14, 22-24). In our study, we also found the frequency of CTS in overt hypothyroidism as 41.9%. This increase in likelihood is also seen in subclinical hypothyroidism, but this difference was not found to be statistically significant. Bilateral CTS was found to be more common in our patient groups compared to the control group. Considering the metabolic nature of hypothyroidism, this is an expected finding.

Literature has mixed reports on the prevalence of PNP in hypothyroidism. Distal sensory complaints were reported in the 29-64% range while the clinical symptoms of PNP were reported with 25-42% of the cases. Electrophysiological findings of PNP, however, are reported in a range of 17-72% of the cases (1, 3, 25-28). Even though the PNP pathogenesis in hypothyroidism is still not fully understood, the mucopolysaccharide accumulation in the endoneurium and perineurium was explained by disease mechanisms such as segmental demyelination, glycogen aggregates, axonal degeneration (15,18,29). While some researchers argued that axonal degeneration is accompanied by secondary demyelination in Schwann cells due to the metabolic anomaly, others suggested that the primary damage is in the axon and that the demyelination develops secondary (15).

In our study, none of the participants fit the criteria for PNP. However, peroneal, tibial, median motor nerve amplitudes were lower in the overt hypothyroidism group compared to the subclinical, and median, peroneal and ulnar motor conductivity velocity were lower compared to both other groups, which could be an evidence for motor bundle involvement. The fact that motor bundles are affected more severely than sensory bundles and that motor bundles connect directly to muscles suggested that the true cause of the pathology is the metabolic pressure in the motor bundles, neuromuscular junction, and muscle cascade due to hypothyroidism. Since the diagnostic criteria for PNP has a certain

level of variability in the literature, the difference in reported PNP findings between the studies is expectable.

In addition to not showing any signs for PNP, subclinical hypothyroidism group had lower amplitude in peroneal CMAP, slower peroneal and ulner MCV and normal sensory conductivity when compared to the control group. Even though it was not as pronounced as the overt hypothyroidism group, the subclinical group also showed some difference in the motor amplitude and conduction velocity. According to our results, overt hypothyroidism shows an obvious involvement of the motor bundles and this is also somewhat visible in subclinical hypothyroidism using electrophysiological measures.

A number of other studies also showed an increased risk for peripheral neuropathy in hypothyroidism (25,31). In contrast with our findings, there are studies showing a bigger involvement of the sensory bundles (3,26,32) but the group sizes of these studies are smaller than the present study. In a study by El Salem on 23 hypothyroidism patients who were neurologically asymptomatic 52% showed motor demyelination-related abnormalities and 30% showed CTS. According to El Salem's study, the primary involvement is on the motor median nerve and the secondary one is on the peroneal nerve. In the needle EMG studies of these patients, 74% showed myopathic MUP. In our study, however, only two patients showed myopathy. The subclinical hypothyroidism and control groups did not show any myopathy.

In conclusion, we found a significantly high likelihood of CTS in the overt hypothyroid group as shown by electrophysiological measures. In the subclinical hypothyroid group, there was a visible increase in CTS even though the difference was not significant. Despite the fact that the criteria for PNP were not met for any patient in the subclinical and overt hypothyroid groups, we observed statistically significant differences in motor amplitude and conduction velocity as compared to the control group. These findings suggest that motor bundles are affected more drastically than the sensory ones.

Since the thyroid replacement therapy can effectively alleviate the motor bundle and neuromuscular junction involvement due to slow basal metabolism in hypothyroidism, we believe further studies are needed to compare the post-treatment electrophysiological findings to pre-treatment assessments and conduct clinical evaluation.

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