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SYMPATHETIC DYSFUNCTION IN PATIENTS WITH DIFFERENT SEVERITY OF CARPAL TUNNEL SYNDROME

FARKLI DÜZEY KARPAL TÜNEL SENDROMLU HASTALARDA SEMPATİK DİSFONKSİYON

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ABSTRACT

Objective: Carpal tunnel syndrome (CTS) is an entrapment mononeuropathy of the median nerve at the wrist. Recently, it was reported that in the entrapment neuropathies, which involved motor and sensorial fibers, autonomic impression might occur. The aim of this study was to investigate the relationship between electrophysiological severity of CTS and sympathetic dysfunction, using the sympathetic skin response (SSR).

Material and methods: Fifty patients with CTS and 34 healthy subjects were enrolled to the study. Patients were divided into mild or severe CTS groups in terms of electrophysiological findings. SSR values were measured in all subjects who enrolled in the study.

Results: All motor and sensory nerve conduction parameters were affected in severe CTS; there were statistically significant differences than the controls ($p<0.01$). SSR latency in severe CTS group was more delayed than mild CTS and controls ($F=6.1$, $p<0.005$). SSR latency were correlated with median nerve peak distal sensory latency, the difference between median and ulnar nerves' peak distal sensory latencies and median nerve distal motor latency in severe CTS group ($p<0.000$, $p<0.000$, $p<0.005$, respectively).

Conclusion: These results suggested that there was sympathetic fibers' involvement beside motor and sensory fibres in CTS and sympathetic involvement became clear when the entrapment was increased.

Key words: Carpal tunnel syndrome, Sympathetic skin response, EMG

ÖZET

Amaç: Karpal tünel sendromu (KTS) median sinirin el bileği seviyesindeki tuzaklanma mononöropatisidir. Son dönemde motor ve duysal sinir liflerini etkileyen çeşitli tuzak nöropatilerinde otonomik tutulumun da olabileceği belirtilmektedir. Bu çalışmanın amacı, KTS'li hastalarda elektrofizyolojik açıdan tutulum şiddeti ile sempatik disfonksiyon arasındaki ilişkinin sempatik deri yanıtları (SDY) kullanılarak araştırılmasıdır.

Gereç ve yöntem: Klinik KTS tanısı konan 50 hasta ile 34 sağlıklı kişi çalışmaya dahil edildi. KTS hastaları, elektrofizyolojik değerlere göre hafif ve ağır KTS olarak iki gruba ayrıldı. Çalışmaya alınan tüm olguların SDY'lerine bakıldı.

Bulgular: Ağır düzeyde etkilenmiş gruptaki bütün motor ve duyusal sinir ileti değerlerinde etkilenme olup, kontrol grubuna göre istatistiksel olarak anlamlı farklar vardı ($p<0,01$). SDY latansı ağır etkilenmiş grupta, hafif etkilenmiş ve kontrol grubuna göre daha uzundu ($F=6,1$, $p<0,005$). SDY latansı, ağır KTS grubunda, median sinir tepe distal duyusal latans, median ve ulnar sinir tepe distal duyusal latans farkı ve median sinir distal motor latansları ile korele idi (sırasıyla, $p<0,000$, $p<0,000$, $p<0,005$).

Sonuç: Bu bulgular KTS'li hastalarda median motor ve duyusal liflerin tutulumununa sempatik lif tutulumun da eşlik ettiğini ve sempatik tutulumun tuzaklanma düzeyi arttıkça belirginleştiğini göstermektedir.

Anahtar kelimeler: Karpal tünel sendromu, sinir ileti çalışması, sempatik deri yanıtı

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INTRODUCTION

Median nerve entrapment at the wrist is the most common mononeuropathy encountered in clinical practise (1). Cardinal symptoms of carpal tunnel syndrome (CTS) include dysesthesia and motor disturbance in the median nerve territory, beside of these symptoms some sympathetic involvement symptoms like swelling in the whole hand or in the fingers were shown. Some patients with CTS have eczematous lesions caused by complete anhydrosis, red or purple discoloration and feeling cold, such as autonomic symptoms were reported in the disease (2,6,11,17,19,24,28).

Various methods have been assessed for their ability to detect autonomic dysfunction in CTS. One of them is sympathetic skin response (SSR) that considered an index of function of the sympathetic pathways and abnormalities have been reported in a variety of disorders of the central and peripheral nervous system (7,8,20,23,26). SSR is defined as a transient change in the electrical potential of the skin that is elicited by internal or external stimuli, and non-invasive, reliable, easily applied test to assess reflex sympathetic activity (21,22). SSR is thought to reflect activity of eccrine sweat glands and adjacent epidermal tissue elicited via postganglionic unmyelinated fibres of the sympathetic sudo-motor system (18).

SSR abnormalities in CTS have been reported previously (2,6,11,12,17,19,24). In CTS, certain changes were expected in SSR because median nerve carries postganglionic unmyelinated fibres (16). In this study, we aimed to assess the correlations between severity of CTS and autonomic dysfunctions with the evidence of SSR evaluation.

MATERIAL and METHODS

Fifty consecutive patients with idiopathic CTS were enrolled to our study from the patients who attended electrophysiology laboratory. Thirtyfour age and gender matched healthy subjects were used as controls. All subjects signed informed consent before participating.

The following criteria have been used in the electrophysiological diagnosis of CTS (10) and hands divided into two groups by electrophysiological criteria: Hands with median distal sensory latency longer than 3.2 msec, the difference between median and ulnar nerves' peak distal sensory latencies longer than 0.5 msec at the 4th finger, or median nerve sensory conduction velocity slower than 50 m/s in wrist segment were grouped as the mild CTS group. The hands with median distal motor latency longer than 4.2 msec with or without abnormality of nerve sensory conduction study were grouped as severe CTS group.

Cases that have been diagnosed with polineuropathy, plexopathy, radiculopathy or proximal compression syndrome through clinical and/or electrophysiological examination have not been enrolled in the study.

The patients were informed about what they should be carefull a day before EMG (i.e. limiting the caffeine consumption, sleeping well). The electrophysiological tests were performed in a semi-darkened and silent room. During the testing, all patients were lying in supine position. Room temperature was maintained at 23^{0}C and bilateral palmar temperatures were verified to be greater than 32^{0}C. And if they were below 32^{0}C, the limbs were heated up by covering with a blanket. ESAOTE electroneuromyography device was used in electrophysiological assessment (a). All patients had median and ulnar motor and sensory nerve conduction studies performed in addition to a needle EMG examination of pertinent median-innervated muscles. In nerve conduction studies, sweeping speed was 50msec/div., 10msec/div., 10-100msec/div.; sensitivity was 5mv/div in motor, 20µv/div in sensory nerve conduction studies and 100- 1000 µv /div in the needle EMG.

In median nerve sensory conduction studies, stimuli were given in the 2nd finger and recording electrodes were set at 12 cm distance to the volar surface of the wrist. In motor nerve studies, stimuli were given at the wrist and elbow and recording over the abductor pollicis brevis muscle at 8 cm distance. In the examination of 4th finger, stimuli were given from the 4th finger with ring electrodes and recording at 11 cm distance to palmar surface of the wrist over the median and ulnar nerves. In studies of ulnar nerve conduction, stimuli were given at the 5th finger and recording at 10 cm distance to volar surface of the wrist, palmar stimulation in hand palmar surface 4th metacarpal space and recording in 8 cm distance to wrist volar surface. Surface electrodes have been used in stimulation and recording.

Six mm disc electrodes were used for SSR recordings. To stimulate median nerve at the wrist, active electrode was placed on the palm, reference electrode on the dorsum of the hand, and ground electrode on the forearm. SSR in patients with CTS was recorded on the involved hand after stimulation of the ipsilateral median nerve and on the healthy hand after stimulation of the ipsilateral median nerve. To avoid habituation, stimulations were made with random intervals and various intensities. A sensitivity of 500µV-2mV per division and sweep speed of 1-2 sec was used. Low-and high-frequency filters were adjusted to between 0.1 and 1000 Hz. The duration of the stimulus was between 0.1 and 0.2 msec and the stimulus intensity ranged 10 mA to 40 mA. If we could not elicit any response to 10 consecutive stimuli, the response was accepted to be absent. The latency was measured from the onset of the stimulus artifact to the first deflection of the signal baseline and the amplitude was measured from peak to peak.

Statistical analyses were performed with the Statistical Package for Social Sciences (SPSS 13.0) software (b). Means of multiple independent groups compared with one-way ANOVA and means of two independent groups compared with Post Hoc Multiple Comparision test. Differences with p values less than 0.05 were considered statistically significant.

RESULTS

The mean age was 48.77±7.78 years in the patients and 47.29±7.85 years in the controls. Table 1 shows the demographic and the mean median sensory and motor nerve conduction values of patients and controls.

Table 1. Demographic and electrophysiologic results of controls and patients with CTS (mean ± SD).

Variables	Patients		Controls	P*
Gender (men/women)	3/47		3/31	0.549
Age (years)	48.77±7.78		47.29±7.85	0.543
Electrophysiology (Median nerve)*	Mild	Severe		
PDSL (ms)	2.78±0.20	3.72±0.41	2.43±0.18	<0.000
SNAP-amp. (mV)	45.90±18.76	11.85±6.11	49.73±20.84	<0.000
DML (ms)	3.78±0.26	5.65±0.91	3.24±0.41	<0.005
CMAP-amp. (mV)	12.68±1.37	6.09±4.91	13.22±5.58	<0.001
PDL-diff. (ms)	0.86±0.12	1.14±0.27	0.32±0.07	<0.001
SCV(m/s)	43.80±5.91	39.65±6.47	55.61±6.84	<0.000

**ANOVA*
PDSL: Median peak distal sensory latency.
SNAP-amp: Median sensory nerve action potential amplitude.
DML: Median distal motor latency.
CMAP-amp: Median compound muscle action potential amplitude.
PDL-diff: The difference between median and ulnar nerves' peak distal sensory latencies from the 4th finger.
SCV: Median sensory conduction velocity.

All sensory and motor nerve latencies in severe CTS group were significantly different longer (F=10.02, p<0.000 and F=6.1 p<0.005) than mild CTS group and controls. In the mild CTS group; median nerve peak distal sensory latency (PDSL), the difference between median and ulnar nerves' peak distal sensory latencies (PDL-diff) from the 4th finger was longer and median nerve sensory conduction velocity (SCV) was slower than controls (p<0.008 and p<0.001).
The SSR data of 50 patients and 34 controls are shown in Table 2.

Table 2. SSR latency in controls and patients with CTS$^{\alpha}$ (mean ± SD).

Patients with CTS	n	SSR latency (ms)
Mild affected groups	20	1.27 ± 0.13
Severely affected groups	30	1.36 ± 0.15
Controls	34	1.26 ± 0.12

** p<0.005*

SSR latency in severely affected group was longer than mild affected group and controls (p<0.003). Correlation analysis was performed on the SSR latency and sensory, motor nerve conduction values (Figure 1).
SSR latency was correlated with PDSL, DML and PDL-diff (r=0.37, p<0.000; r=0,38 p<0.000 and r=0.30, p<0.005, respectively).
Normative values (1.26±0.12 ms, mean ± SD) for SSR were established in 34 hands. Normative values for SSR and median nerve latencies in mild and severe CTS were shown in Figure 2.

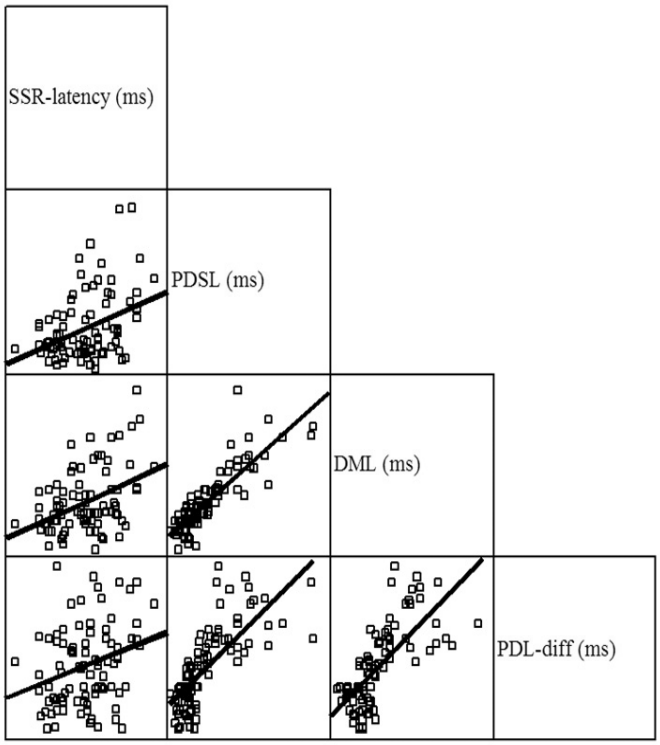

Figure 1.Correlation analysis of SSR latency with sensory and motor nerve conduction values
Foot note for Figure-1: *SSR-latency: Sympathetic skin response latency, PDSL: Median peak distal sensory latency, DML: Median distal motor latency, PDL-diff: The difference between median and ulnar nerves' peak distal sensory latencies from the 4th finger.

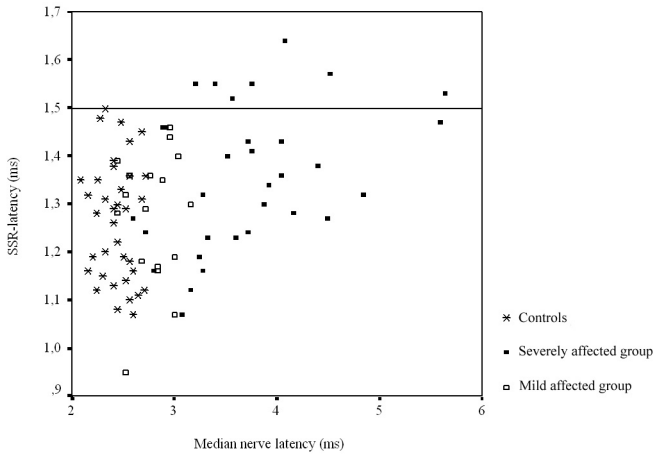

Figure 2. Normative values for SSR and median nerve latency in CTS

The response was considered abnormal if the latency exceeded 1.50 ms (>2SD). We found 7 patients with abnormal SSR latency and all were in the severe CTS group.
The power value of the study was found as 0.99 in post-hoc power analysis of SSR latencies between the patient and the control groups.

DISCUSSION

SSR is thought to reflect activity of eccrine sweat glands and adjacent epidermal tissue elicited via postganglionic unmyelinated fibres of the sympathetic sudomotor system (18). SSR might therefore serve as an indicator of autonomic dysfunction in CTS, because median nerve carries postganglionic unmyelinated fibres (6). Axonal neuropathy correlated strongly with the absence of SSR; conversely those with predominantly demyelinating neuropathy had intact responses (21,22). Initially regarded as an "all-or-none phenomenon," refinements in recording techniques have established normative data for both SSR amplitudes and latencies (3,4,9,14). In our study, there were no electrophysiological findings, which reflected severe axonal neuropathy with needle EMG records from the abductor pollicis brevis muscle. This may be explained that SSR were recorded in the all patients.
Recent studies have reported abnormal SSR amplitudes and latencies in patients with diabetic neuropathies compared to normal controls (5,25,27). Severity of the neuropathy reflected that the degree of abnormality on the SSR, with 32% of the patients with mild neuropathy showing increased SSR latencies in the hand compared to 48% of patients with severe neuropathy (5). In our study, prolonged distal latencies, SNAP and CMAPs with lower amplitudes were recorded in severe CTS group, according to mild CTS and control groups, it suggested that there were severe focal demyelinating neuropathy on median nerve sensory and motor fibers. SSR latencies in severe CTS group were prolonged significantly more than mild CTS and control groups. SSR latency can be used as an index to determine of the severity in the sensory and motor neuropathy. Positive correlation between SSR latency and PDSL, DML PDL-diff was considered the involvement of unmyelinated sympathetic efferents related to median nerve sensory and motor focal demyelinative neuropathy in CTS. Seven patients with abnormal SSR latencies were all in severe CTS group, which suggested, that severely affected median nerves were needed for the involvement of unmyelinated sympathetic efferents.
Caccia et al. (6) and Reddeppa et al. (17) compared controls and patients with CTS, and found a decrease in the SSR areas of the affected hands. In some studies no significant difference were found between the SSR parameters in the control and CTS groups (2,15,19). Argyriou et al.'s study on the severity of CTS and SSR does not support our results too (2). The researchers had got normal SSR even on severe CTS. In fact, low diagnostic sensitivity and limited clinical significance of SSR examination in patients with CTS were suggested in some previous studies (19). But in another study (24), symptoms of autonomic dysfunction, that compared electrophysiological assessments in CTS and the severity of illness, there was a significant statistical relation between the symptoms of autonomic dysfunction and SSR's. Bayrak et al showed axonal loss by motor unit number estimation despite no significant SSR difference between control and CTS groups found (15). These different results may be explained by a study, that nerve conduction investigations were shown a highly sensitive procedure, reflects pathology, independent of the severity of the clinical involvement (13). However, current knowledge on sympathetic involvement in CTS is not enough to provide a definitive determination of its magnitude and clinical importance (28).
Our study has some limitations, like small sample size, gender predominance and inappropriate planning in data collection so that reason this should be studied in a larger group. Our groups consisted predominantly of women. Community based studies suggest that there is a female preponderance in CTS but healthy women have autonomic symptoms, too (4). Therefore, male individuals with CTS may be studied in large series. In the future studies, detailed symptoms' records are needed.
Early diagnosis by a trained professional combined with proactive treatment to minimize damage is important to prevent the progression of the CTS. SSR was found correlated with severity of CTS in our study, as for the diagnostic value of SSR that may be used by clinicians in their evaluations. In the light of our results, making comprehensive documentation of CTS which contains SSR studies seems to be one of the important issue to build a accurate evaluation of the CTS.

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