Electrophysiological Study Of The Effect Of Posture On The Sympathetic Skin Response In Normal Subjects And In Diabetic Patients

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Abstract:

Thirty nine diabetic patients, of both insulin dependent and noninsulin dependent types, and thirty four age and sex matched control subjects were included in this study in an attempt to clarify the effect of changing posture on the peripheral nerves in both groups and to clarify the effect of diabetes on the peripheral nerve by using electromyography.

Peripheral nerve dysfunction was evaluated by clinical examination, and electrophysiological testing of the somatosensory and autonomic peripheral nerves in supine and in standing position.

The sympathetic skin responses (SSR) evoked by electrical stimulation of right and left median nerves and right and left common peroneal nerves were also recorded and analyzed.

The sympathetic skin response test of diabetic patients show a significant reduction in latency and amplitude of the SSR in both upper and lower limbs with more affection in the lower limbs, and it was absent in 7 patients in upper and lower limbs, and in 13 patients in lower limbs only. Also there is a significant reduction in the amplitude of SSR in both upper and lower limbs.
control and diabetic groups on standing from supine position. Lastly, we conclude that the electrophysiological assessment of the peripheral nerve is essential for the diagnosis of the peripheral neuropathy which often accompanied with diabetes mellitus. Also we found that the abnormal SSR indicates the early affection of small unmyelinated c fibers in case of diabetic neuropathy. Also, we found that the sympathetic nerve fibers are significantly affected by changing body posture from supine to standing position.

Introduction:
Quantitation of autonomic sudomotor function provides important information on peripheral autonomic failure in diabetic neuropathy. It complements the evaluation of measurements of motor and sensory deficits (Dyck and Thomas, 1999). In the conventional nerve conduction studies, unmyelinated fibers do not contribute to the surface recorded responses. Recording sympathetic skin response using a non-invasive technique provides a means to test these axons (Kimura, 2001).

Other tests are mostly based on cardiovascular reflexes. Most of these tests involve measurement of changes in heart rate in response to various stimuli. They are predominantly tests of vagal function and may not identify individuals in whom the abnormality lies within the sympathetic nervous system. The occurrence of postural hypotension is an indicator of sympathetic failure but it is a late phenomenon in diabetic neuropathy.

Sympathetic skin response is a transient change in the electrical potential of the skin, reflexively evoked by a variety of internally generated or externally applied stimuli (Drory, and Orczy, 1993). This test demonstrates the change in voltage measured from the surface of the skin, after electrical stimulation of peripheral nerve afferents or deep inspiration and this change is also a predictor of sudomotor activity. When elicited by electrical stimulation, the response uses a reflex arc, which includes large myelinated sensory fibers as an afferent limb, central relays in thalamus and efferent sympathetic pre- and postganglionic nerve fibers, which postganglionic ecrine sweat glands in the skin (Drory, and Koezyn, 1993). The latency of the response is mostly determined by conduction in the efferent small unmyelinated fibers (Ozge, Saracoglu, Gurtekin, et al., 2000). The response amplitude varies widely and has a marked tendency to habituate. The amplitude is larger in the upper than in the lower limbs (Navarro et al., 1993).

Patient with diabetes have absent or reduced response on the affected limb (Kimura, 2001). In diabetic neuropathy Watahiki et al (1989) found that the decrease in the SSR amplitude correlated well with a fall in motor and sensory conduction velocity. They also found that the magnitude of the SSR correlated well to the impaired R-R interval variation during deep breathing, heart rate increase, and blood pressure change on standing indicating a close correlation between the disturbance of sudomotor function and that of other sympathetic and parasympathetic functions (Vital, LeBlanc, Vallat, et al., 1994). Nazhe et al (2002) believe that measurement of the SSR latencies is an objective measure of conduction in a long multineuronal pathways and can detect subclinical involvement of sympathetic nervous system in diabetics who do not manifest symptoms or signs referable to autonomic system dysfunction (Nazhe, Yetkin, Irkec, and Kocer, 2002).
Materials and Methods:

Subjects: Two groups of human subjects were included in the present study. Electroneurographic tests were carried on the two groups, i.e. the control and the patient groups. Electrophysiological studies were performed in the Neuropysiology Units/Department of Physiology in Al-Sadr Teaching Hospital at Al-Najaf and Marjan Teaching Hospital at Hilla City.

The control subjects: Thirty four healthy volunteers were included in this study (19 males and 15 females). The age of this group ranged between (19 and 70 years) with a mean of (37.53 ± 10.88) years. Their social status ranged between doctors, medical students, hospital working staff and other volunteers.

The subjects included in this study have the following criteria:

A. Non diabetic (FBS was <110 mg/dl (6.1 mmol/l).
B. No evidence of neurological disease.

All of them were instructed and informed about the aim of the study and investigation procedures and their acceptance was taken.

The patients: Thirty nine patients whom are a known cases of diabetes mellitus (DM) of both (insulin dependent and noninsulin dependent DM) of both sexes (males and females), their ages ranging between (21 and 70 years) with a mean of (47.9 ± 14.4) years.

All those patients were referred to the unit of neuropysiology after being diagnosed by a specialist. All the patients were on treatment (oral hypoglycemic agents or insulin injection). Their disease duration ranges from 5 months to 25 years with a mean duration of (8.23) years. All of them have no history of alcoholism, renal or other metabolic diseases identified on a medical questionnaire.

As the control subjects, they were informed about the aim of the study and investigation procedure and their acceptance were taken.

After full medical history and clinical examination all the subjects underwent electrophysiological study.

Methods: All subjects were investigated by the sympathetic skin response of both right and left upper and lower limbs which was performed in both supine and standing positions for both patients and control subjects.

The test procedure was explained in brief for each subject in order to alleviate any fear, anxiety, or apprehension that may be present in the subject. All the subjects were examined in the morning, at a room temperature of 25 to 28 °C, and they were kept in this room for at least 15 minutes before being electrophysiologically examined, and their skin temperature ranged between 30 and 34 °C(measured by a digital thermometer inserted between the index and the middle finger).

Instrumentation:

The EMG machine: Micromed Systemplus digital system was used for all the electrophysiological analysis of sensory, motor nerve conduction parameters and sympathetic skin response. The Micromed Systemplus is four-channel equipment which is designed to have a wide range of applications in the field of electrophysiological testing and clinical neurophysiology.

This system includes two sets of four channels preamplifiers and two isolated stimulators with separate jacks (A and B).

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A group of controls in the keyboard of the system is used for setting the stimulus intensity (1-99 MA), duration (0.05-1 msec), polarity (positive, negative, and alternate), and frequency of its presentation (0.1-100 Hz), these can also be set by using the mouse of the system. The evoked responses can be displayed on the monitor, on which the four channels can be displayed at the same time. The results are printed in laser shoot printer associated with the machine on A4 type papers to obtain permanent recording of the displayed signals, and a copy of the results of each examined subject is stored in the memory of the system to be ready if we need it later on. The machine also contains an audioamplifier, the audioamplification during needle examination helps in the recognition of much potential by their characteristic sounds.

A group of controls in the keyboard is used to adjust the amplification (sensitivity), sweep speed (time scale), and the various measurement of the displayed signals, which can also be adjusted by using the mouse of the system.

The Electrodes:

A. Grounding Electrode: A Velecro ribbon strapped surface-grounding electrode (Micromed) was used to protect the subject against electrical hazard and to reduce artifacts and interference. The electrode was soaked in normal saline before use, to ensure good electrical conduction.

B. Stimulating Electrodes: A bipolar surface stimulating electrode (Micromed) was used to stimulate motor nerves through the skin. The electrode consists of two felt tips mounted in the stainless steel holders in a plastic frame. Center to center between the felt tips is 23 mm each felt tip diameter is 6 mm. The felt tips were soaked in normal saline before use to ensure good conduction. They were applied manually on the skin over the nerve to be tested. The cathode of the stimulation electrode was indicated by the sign of minus (-), and the anode was indicated by the sign of plus (+).

C. Recording Electrode: A pair of circular plates of silver chloride (7mm in diameter) (Micromed surface recording electrode) were used as recording electrodes (called surface bipolar electrodes) of SSR. The surface bipolar electrodes were fastened to the skin with sticking plaster and an electrode paste (Micromed -paste) was used to ensure good electrical contact between skin and electrodes. These surface electrodes were connected to the amplifier by an electrode cable (Micromed loop connecting cable). Before application of these electrodes, the skin was cleaned by spirit and.

The Micromed Systemplus EMG system has a specific program for SSR recording and analysis. In our study the SSR was performed with the subjects lying supine and relaxed in a semi-darkened, air-conditioned room, then we perform it in the same conditions but with the subjects in a standing position (the recording in both positions was from the right and left upper and lower limbs). External stimuli were avoided as much as possible. During the recording, the ambient temperature was maintained around 30°C and the temperature of the skin of the palm of the hand and the sole of the foot above 32°C. SSR from the upper limbs was elicited by stimulating the right and left hand at the wrist or any digit (median nerve), while from the lower limbs by stimulating the foot at the ankle or any digit (common nerve).
The procedure:

A. In supine position: While the subjects lying on the couch in supine position for 3-5 minutes; the sympathetic skin response test was performed for both upper and lower limb in all subjects.

The upper limb:

Recording electrodes: The active surface electrode was placed in the center of the palm of the hand with the reference electrode on the dorsum of the hand.

Grounding electrode: A Velcor ribbon strap surface grounding applied around the wrist between the stimulating and the recording electrodes.

Stimulating electrode: The stimulating electrode was placed over the median nerve at the wrist between the tendons of the Palmaris longus and flexor carpi ulnaris muscles (Ozge A, Saracoglu M, Gurtekin Y, et al, 2000). The stimulus intensity also can be applied to the ipsilateral or contralateral wrist or any digit (Kimura, 2001).

The lower limbs:

Recording electrode: The active surface recording electrode was placed on the planter surface of the foot in the center of the sole. The reference electrode was placed on the dorsum of the foot.

Grounding electrode: A Velcor ribbon strap surface grounding applied around the ankle between the stimulating and the recording electrodes.

Stimulating electrode: The bipolar stimulating electrode is applied either at the ankle, lateral to the tibialis anterior tendon, proximal to the lateral malleolus, or at any digit.

The electromyographic setting for SSR was:

Frequency: 0.1/10 Hz
Sweep speed: 0.5-1 s/Div
Sensitivity: 100µV/Div
Stimulus intensity: 10-20 mA

With a short duration of stimulation (1 msec).

B. In standing position: After standing from supine position for 3-5 minutes, the same procedure as in standing position was performed for recording the SSR.

The following parameters were taken into consideration for the evaluation of the responses:

1-Onset latency (sec).
2-Amplitude (µV).
3-Duration (sec).
4-Area (µVs).

The most important of these are the onset latency (which reflects the conduction in postganglionic C fibers) and the amplitude (which reflect the density of the spontaneously activatable sweat gland or the neuroglandular junction) (Kimura, 2001).

Results:

The general clinical data of the subjects included in this study is shown in the table (1). There is no considerable number of hypertensive and ischemic heart disease cases in both studied groups.
The diabetic cases were of both IDDM and NIDDM, and on both insulin and oral hypoglycemic agents.
Table (1): General clinical data of the subjects included in the study

<table>
<thead>
<tr>
<th>Sex</th>
<th>Control Subjects</th>
<th>DM Patients</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>19 subjects</td>
<td>20 patients</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>15 subjects</td>
<td>19 patients</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>37.529 ± 10.8774</td>
<td>47.8974 ± 14.3944</td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>25.2206 ± 2.58466</td>
<td>26.4 ± 3.31583</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>BSA (m²)</td>
<td>1.9361 ± 0.12525</td>
<td>1.8174 ± 0.17476</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>DM Duration (years)</td>
<td></td>
<td>8.23076 ± 5.90143</td>
<td></td>
</tr>
</tbody>
</table>

The sympathetic skin response SSR recorded from the right and left upper limbs was present in 34 out of 34 control subjects (100%), while it was present in 27 out of 39 diabetic patients (69.23%). In the lower limbs (right and left) the SSR was present in 32 out of 34 control subjects (94.12%), while it was present in only 19 out of 39 diabetic patients (48.72%). Paired T-test showed highly significant difference between the diabetic and control group.

Table (1): SSR of right hand

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control Subjects</th>
<th>Diabetic Patients</th>
<th>P1-P2 value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lat. (msec)</td>
<td>Supine 1.06±0.27</td>
<td>Standing 1.12±0.24</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td></td>
<td>Supine 1.17±0.64</td>
<td>Standing 1.103±0.58</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Amp. (mV)</td>
<td>Supine 0.903±0.34</td>
<td>Standing 0.87±0.29</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td></td>
<td>Supine 0.35±0.32</td>
<td>Standing 0.41±0.35</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

The right hand amplitude of control subjects is significantly increased on standing position.

Table (2): SSR of right hand

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Supine</th>
<th>Standing</th>
<th>P1-value</th>
<th>Supine</th>
<th>Standing</th>
<th>P2-value</th>
<th>P1-P2 value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lat. (msec)</td>
<td>1.06±0.27</td>
<td>1.17±0.64</td>
<td>&gt;0.05</td>
<td>1.12±0.24</td>
<td>1.103±0.58</td>
<td>&gt;0.05</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Amp. (µV)</td>
<td>0.903±0.34</td>
<td>0.35±0.32</td>
<td>&lt;0.05</td>
<td>0.87±0.29</td>
<td>0.41±0.35</td>
<td>&gt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

The amplitude of the diabetic patients is significantly lower than that of the control subjects in supine position, with significant difference between the P-values of the amplitude.

Table (3): SSR of left hand

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control Subjects</th>
<th>Diabetic Patients</th>
<th>P1-P2 value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lat. (msec)</td>
<td>Supine 1.14±0.28</td>
<td>Standing 1.19±0.25</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td></td>
<td>Supine 1.23±0.64</td>
<td>Standing 1.09±0.68</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Amp. (mV)</td>
<td>Supine 0.91±0.28</td>
<td>Standing 0.84±0.25</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td></td>
<td>Supine 0.42±0.42</td>
<td>Standing 0.35±0.29</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

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The amplitude of diabetic patients is significantly decreased in standing position, with significant difference between the P-values of the amplitude.

### Table (4): SSR of left hand

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control subjects</th>
<th>Diabetic Patients</th>
<th>P1-value</th>
<th>Control subjects</th>
<th>Diabetic Patients</th>
<th>P2-value</th>
<th>P1-P2 value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lat. (msec)</td>
<td>1.14±0.28</td>
<td>1.23±0.64</td>
<td>&gt;0.05</td>
<td>1.19±0.25</td>
<td>1.09±0.68</td>
<td>&gt;0.05</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Amp. (µV)</td>
<td>0.91±0.28</td>
<td>0.42±0.42</td>
<td>&lt;0.05</td>
<td>0.84±0.25</td>
<td>0.35±0.29</td>
<td>&lt;0.05</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

The amplitude of diabetic patients is significantly lower than that of the control subjects in standing and supine position.

### Table (5): SSR of right foot

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control Subjects</th>
<th>Diabetic Patients</th>
<th>P1-P2 value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lat. (msec)</td>
<td>1.12±0.44</td>
<td>1.31±0.44</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Amp. (mV)</td>
<td>0.73±0.33</td>
<td>0.72±0.32</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

The latency of right foot is significantly decreased in standing position in control subjects and diabetic patients.

### Table (6): SSR of right foot

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control Subjects</th>
<th>Diabetic Patients</th>
<th>P1-P2 value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lat. (msec)</td>
<td>1.12±0.44</td>
<td>0.76±0.82</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Amp. (mV)</td>
<td>0.73±0.33</td>
<td>0.13±0.12</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

The right foot latency and amplitude are significantly lower in diabetic patients than that of control subjects in both supine and standing position, with significant difference between their P-values.

### Table (7): SSR of left foot

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control Subjects</th>
<th>Diabetic Patients</th>
<th>P1-P2 value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lat. (msec)</td>
<td>1.5±0.59</td>
<td>0.81±0.92</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Amp. (µV)</td>
<td>0.81±0.4</td>
<td>0.14±0.17</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

The latency of the diabetic patients is significantly decreased in standing position, with significant difference between their P-values.

### Table (8): SSR of left foot

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control Subjects</th>
<th>Diabetic Patients</th>
<th>P1-P2 value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lat. (msec)</td>
<td>1.5±0.59</td>
<td>1.5±0.48</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Amp. (µV)</td>
<td>0.81±0.4</td>
<td>0.14±0.17</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>
The latency and amplitude of diabetic patients are significantly lower than that of control subjects in supine and standing position, with significant difference between the two P-values of the latency.

P-Value for SSR latency was <0.05, P-Value for SSR amplitude was >0.05
Figure (3-1): Comparison between SSR latency and amplitude of right hand of control subjects in supine and standing position.

P-Value for SSR latency was >0.05, P-Value for SSR amplitude was >0.05
Figure (3-2): Comparison between SSR latency and amplitude of left hand of control subjects in supine and standing position.
P-Value for SSR latency was < 0.05, P-Value for SSR amplitude was > 0.05
Figure (3-3): Comparison between SSR latency and amplitude of right foot of control subjects in supine and standing position.
P-Value for SSR latency was > 0.05, P-Value for SSR amplitude was < 0.05

Figure (3-4): Comparison between SSR latency and amplitude of left foot of control subjects in supine and standing position.

P-Value for SSR latency was > 0.05, P-Value for SSR amplitude was > 0.05

Figure (3-5): Comparison between SSR latency and amplitude of right hand of DM patients in supine and standing position.

P-Value for SSR latency was > 0.05, P-Value for SSR amplitude was < 0.05
Figure (3-6) Comparison between SSR latency and amplitude of left hand of DM patients in supine and standing position.

P-Value for SSR latency was < 0.05, P-Value for SSR amplitude was > 0.05

Figure (3-7): Comparison between SSR latency and amplitude of right foot of DM patients in supine and standing position.

P-Value for SSR latency was < 0.05, P-Value for SSR amplitude was < 0.05

Figure (3-8): Comparison between SSR latency and amplitude of left foot of DM patients in supine and standing position.

P-Value for SSR latency in supine position was > 0.05
P-Value for SSR amplitude in supine position was < 0.05
P-Value for SSR latency in standing position was > 0.05
P-Value for SSR amplitude in standing position was < 0.05
Figure (3-9): Comparison between SSR latency and amplitude of right hand of control subjects and DM patients in supine and standing position.
P-Value for SSR latency in supine position was > 0.05
P-Value for SSR amplitude in supine position was < 0.05
P-Value for SSR latency in standing position was > 0.05
P-Value for SSR amplitude in standing position was < 0.05

Figure (3-10): Comparison between SSR latency and amplitude of left hand of control subjects and DM patients in supine and standing position.

P-Value for SSR latency in supine position was > 0.05
P-Value for SSR amplitude in supine position was < 0.05
P-Value for SSR latency in standing position was < 0.05
P-Value for SSR amplitude in standing position was < 0.05

Figure (3-11): Comparison between SSR latency and amplitude of right foot of control subjects and DM patients in supine and standing position.
P-Value for SSR latency in supine position was < 0.05
P-Value for SSR amplitude in supine position was < 0.05
P-Value for SSR latency in standing position was < 0.05
P-Value for SSR amplitude in standing position was < 0.05

Figure (3-12): Comparison between SSR latency and amplitude of left foot of control subjects and DM patients in supine and standing position.

Discussion:
Diabetic neuropathy is probably the most common diabetic complication. Due to its complexity it is still poorly understood. The underlying mechanism of diabetic neuropathy is of a multi-syndrome effect divided in two categories which are due to either vascular, metabolic or a combination of two (Cameron NE, Cotter MA, 1994, 1997 and 2001).

In this study these two categories are investigated electrophysiologically with especial consideration of postural effects.

In this study the control group is selected to be age and gender matched to the patient group, this is important to exclude the effect of these two factors on clinical and electrophysiological tests. In addition, there was no significant difference in the incidence of smoking habit and cardiovascular disease between the two groups. However, the incidence of hypertension was higher in the diabetic group subjects. Diabetic autonomic neuropathy develops within a short duration of diabetes even when somatic neuropathy is not apparent (Pfeifer MA, 1984).

A simple non-invasive test, sympathetic skin response (SSR) has been used to assess sympathetic function (Shahani BT, Halperin JJ, Boulu P, Cohen J, 1984). SSR provides objective information from small unmyelinated c fibers that can not be assessed by the currently performed electrophysiologic techniques (Caminero A, Jimenez A, Barrerio P, Ferrer T, 1995). The sympathetic skin response SSR measures changes in voltage of the skin surface as a result of activity in the sudomotor fibers triggered by electrical stimulation.

out a high incidence of SSR abnormalities among patients with diabetic neuropathy. Niakan and Harati (Niakan E and Harati Y, 1988) demonstrated absent SSR in the foot in as high as 83% of their diabetics with symptomatic sensorimotor neuropathy. In the series of Soliven and his collaborators (Soliven B, Maselli R, Jaspan J, et al, 1987), absent SSR of the foot was demonstrated in 66.5% of diabetics with symptomatic neuropathy. As to the SSR in the hand, the former reported absence in 37% and the latter in 28% of cases.

In the present series 42% of the patients revealed absent SSR in the hand and 61% of the patients revealed absent SSR in the foot. In our patients the amplitude of the first negative peak of the SSR in the hand was significantly reduced. It was reported that the amplitude is the most important clinical parameter in the SSR test especially in early stages of the autonomic diabetic neuropathy (Shahani BT, Halperin JJ, Boulu P, Cohen J, 1984, Knezevic W, Bagada S, 1885, Baba M, Watahiki Y, Matsunaga M, Takebe K, 1988 and Nazhel B, Yetkin I, Irkec C, Kocer B, 2002).

In this study the finding that the SSR latencies and amplitudes of diabetic patients are generally significantly lower than that of control subjects, goes with finding of other studies.

Early decrease of SSR amplitude can be produced by involvement of unmyelinated post-ganglionic sudomotor fibers, however the absence of SSRs is attributed to the involvement of large myelinated afferent fibers (Maselli R, Jaspan J, Soliven C, et al, 1989).

The significant difference in the latency and amplitude of the SSR between the normal subjects and diabetic patients may be explained by the fact that large myelinated fibers contribute to the sympathetic skin response. Thus, if the number of functional fibers is above a certain threshold, the response will be elicited, albeit with decreased amplitude, and if not, it will be absent (Zgur T, Vodusex DB, Krzan M, et al, 1993).

**Conclusion:**

SSR is a simple and useful method for evaluation of the autonomic function, small unmyelinated C fibers, in peripheral neuropathy. The amplitude of the first negative wave and presence or absence of the responses was the most important parameters. Abnormal SSR in the patients indicates the early affection of small unmyelinated C fibers in diabetic neuropathy. There is a significant reduction in the amplitude and latency of the SSR in diabetic patients in comparison with the control subjects. Also there is a significant reduction in the amplitude of the SSR on standing position in both control subjects and diabetic patients. Since the amplitude is an indicator to the number and size of the functioning axons, we believe that there are less functioning axons on standing position than supine position.

**References:**


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