Original Article

The autonomic dysfunction in patients with lupus disease: An electrophysiological study

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Abstract

Background: The aim of this study was to investigate autonomic nervous system (ANS) function by using electrophysiological tests in patients with systemic lupus erythematosus (SLE).

Materials and Methods: This descriptive analytical study was done on 28 individuals with a history of lupus and ten age- and sex-matched healthy objects were being selected randomly. The autonomy questionnaire has been used to determine clinical symptom of ANS involvement. The electrophysiological assessments of ANS function were performed by sympathetic skin response (SSR). The mean values of sympathetic (SSR latency and amplitude) parameters were compared to determine any correlations between SSR parameters and clinical characteristics of ANS.

Results: 28 SLE patients (3 males, 25 females) with a mean age of 34.6 ± 9.74 years and 10 control subjects (4 males, 6 females) with a mean age of 36.8 ± 6.43 years were included in the study. Among patients 17 (60.7%) exhibited autonomic symptoms. Headache was the most common issue with the highest percentage rate (41.17%). The mean latency and amplitude of SSR were increased (1.52 ± 0.16 vs. 1.39 ± 0.16 and 107 ± 15.6 vs. 110 ± 15.6, respectively), compared to control. A significant difference was observed between the SSR test results of patients with lupus compared to normal healthy objects ($P < 0.05$). $R = 0.43$ correlation was found between autonomy questionnaire scores and SSR ($P < 0.05$).

Conclusion: It could be concluded that latency measures in SSR test can be used as a valuable and accurate evaluation guideline for autonomic system assessment.

Key Words: Autonomic nervous system, lupus, sympathetic skin response

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INTRODUCTION

Systemic lupus erythematosus (SLE) is an autoimmune disease of unknown etiology affecting multiple organ systems, including the skin, joints, kidneys, heart, and nervous system. Neuropsychiatric SLE is one of the most important manifestations of SLE[1-3] that targets the central, peripheral, and autonomic nervous system (ANS). The reported frequency of central nervous system (CNS) involvement is 11–60% while the peripheral nervous system (PNS) is involved in 2–18% cases.[1,4] Generally speaking, disseminated SLE disease referred to as, lupus is a chronic autoimmune disease affecting various

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organs and body sites such as skin, joints, blood, and kidney. Chronic signifies the disease and can tend to last longer than usually affect the body parts, and autoimmune means the immune system attacks body tissues instead of protecting the body against bacteria and viruses. Fertile women of age group 15–45 years are more prone to the disease and the rate of incidence is 9-1 for females versus males, showing women are at higher risk of experiencing the disease compared to the same male age group. However, the disease is more common among the younger age group of boys compared to girls before puberty. SLE has been evidenced among world population; however, the disease is observed more among American, Spanish, and Asian races. The base for disease diagnoses is CNS involvement and joint inflammation (arthritis). Most patients with SLE suffer from arthritis. Arthritis causes pain and inflammation of joints in hands, wrists, elbows, knees, and many other body parts joints. Laboratory testing is available to identify the various involved body parts. Among these tests, we can point out sympathetic skin response (SSR) known as SSR. SSR considers an electrophysiological technique and polysynaptic process related to sweat glands.[5,6] Recording SSR is a simple and useful method for assessing PNS, which may not be possible to be assessed by common electrodiagnosis techniques.[7] SSR defines based on instant alterations in skin electrical potential by external and internal stimuli on peripheral nerves such as deep breath, painful stimuli, and electrical stimuli.[8] One of these less perceived and applicable issues is the use of SSR in patients affected with lupus. However, studies that have evaluated ANS function in SLE are not common, and most of them analyzed ANS dysfunction using various methods and indicated conflicting results with different degrees of involvement.[2,9,10] Therefore, the aim of this study was to investigate ANS function by using electrophysiological tests in patients with SLE and determine the extent of autonomic system involvement among patients diagnosed with lopus and the possibility of association with abnormal electrophysiological tests.

MATERIALS AND METHODS

The research was a descriptive analytical study. Twenty-eight individuals with a history of lupus and 10 age- and sex-matched healthy objects were being selected randomly. The autonomy questionnaire has been used to determine clinical symptom of ANS involvement. The electrophysiological assessments of ANS function were performed by SSR [Figure 1]. The mean values of sympathetic (SSR latency and amplitude) parameters were compared and any correlations between SSR parameters and clinical

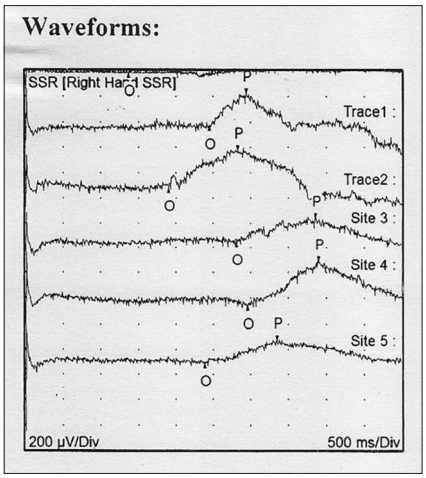

Figure 1: An example of waveforms

disease characteristics were determined. None of the objects had allergy reaction, diabetes or being pregnant, or have any sign and symptom of specific disease that impact ANS response and sympathetic response test such as rheumatoid arthritis, hypothyroidism, and hyperthyroidism, taking B-blocker drugs, trichloroacetic acid, diuretics, nitrofurantoin, alcohol, and uremia. For assessing the normal range of SSR and for assurance of normal range for our control subjects (10 people) Domitro books were been used which provided the conformity for results. Data analysis was accomplished by use of SPSS 20 software IBM SPSS CO. $P < 0.05$ was considered as the significance level.

Testing methods

Method of testing was as follows: After choosing control and study experimental groups, they were placed in a quiet room with a pleasant temperature in a sitting position with a skin temperature between 34°C and 36°C. The electrodes were been connected and fixed in appropriate places after cleaning hand sites with cotton and alcohol. Active electrode was placed in the middle finger of right hand and fixed electrode was placed on volar of the right hand wrist, and in next step the palm electrode was connected to earth. For recording SSR fluctuations, a physiograph device made in Iran was used, which is shown in Figure 2. The stimulation was done in 0.002 of second manually and in every 30 s periods for the prevention of getting used to theestimulations. For every sample, we recorded 10 SSRs. For SSR curve evaluation, the amplitude of the curve and latency in each 10 curves was measured and recorded by the software and all responses, mean, and standard deviation (SD) parameters were being obtained. Latency of the stimulation artifact site for the first curve location of the isoelectric line was considered and expressed based on second. Curve domain was also defined

Figure 2: Physiograph device

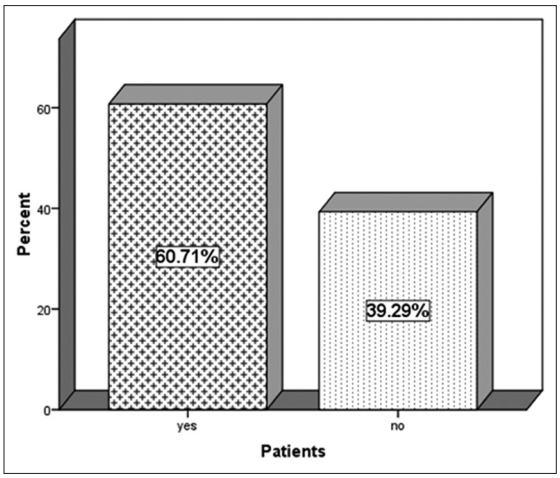

Diagram 1: Frequency percentage of patients with regard to neurological complications

from the positive peak point to lowest negative point and expressed by microbial after calculation and conversion of units.

RESULTS

Twenty-eight SLE patients (3 males, 25 females) with a mean age of 34.6 ± 9.74 years and 10 control subjects (4 males and 6 females) with a mean age of 36.8 ± 6.43 years were included in the study. Taking into account [Table 1 and Diagram 1], it could be observed that 60.71% of patients are affected by neurological complications, and only 39.29% did not show these signs and symptoms. The complications were specified in Table 2 for patients affected by these signs and symptoms in which headache was the most common issue among them and highest percentage rate (41.17%).

As you can see from Table 3 correlation between autonomy questionnaire scores and SSR was 0.02 statistically significant ($P < 0.05$).

In each group, we evaluated the age and the rate of women to men. No significant statistical difference was observed for age, but there was a significant statistical difference for gender. The results have been shown in Table 4.

Latency value was statistically significant for two groups ($P < 0.05$). Amplitude of SSR was also significantly different. In fact, SSR showed significant difference in lupus group and control healthy group. Mean and SD of SSR response are shown in Table 5.

Table 1: Frequency of patients with neurological complications

Neurological signs and symptoms	Frequency (%)
Yes	17 (60.71)
No	11 (39.29)

Table 2: Frequency of main neurological complications

Valid	Frequency (%)
Headache	7 (41.17)
Dizziness	5 (29.41)
Both	5 (29.41)
Total	17 (100.0)

Table 3: Correlation

SSR	Autonomy questionnaire scores
Pearson correlation	0.43
Significant (two-tailed)	0.02

SSR: Sympathetic skin response

Table 4: The basic information for healthy objects and patients with lupus

Index	Average		*P*
	Control healthy group (*n*=10)	Experimental group with lupus (*n*=28)	
Age (year)	36.3	34.87	>0.05
Rate of women to men	0.36	0.87	<0.05

Table 5: Latency value and amplitude of response for healthy control group and patients with lupus

Index	Average±SD		*P*
	Control healthy group (*n*=10)	Experimental group with lupus (*n*=28)	
Latency (S)	1.39±0.16	1.52±0.16	<0.05
Amplitude of SSR (mv)	107.35±15.55	110.45±15.55	<0.05

SD: Standard deviation, SSR: Sympathetic skin response

DISCUSSION

SLE affects all limbs of the nervous system. Studies that have evaluated ANS function in lupus disease (SLE) are rare and have indicated different degrees of involvement with some authors even reporting

the absence of any significant ANS dysfunction in lupus.[2,3,5-10] This may be because symptoms of autonomic dysfunction are nonspecific and extremely varied. Moreover, tests to detect autonomic dysfunction are not routinely employed in clinical practice.[11] Shalimar *et al*. assessed autonomic dysfunction in systemic lupus erythema using a comprehensive questionnaire reported nearly one-third of their patients (37.2%) exhibited one or more autonomic symptoms with nasal symptoms being the ones most frequently encountered and 6 (12%) patients had significant symptoms.[12]

According to our data, we have determined that 60.71% of our patients are affected by neurological complications, and only 39.29% did not show these signs and symptoms in which headache was the most common issue among them and highest percentage rate (41.17%) In this study, a significant difference was observed between recorded SSR latency value of patients affected by lupus and healthy control group. The SSR is a slow wave resulting from activation of the sudomotor sympathetic efferent fibers. Records are usually made with surface electrodes on hand or foot after the electrical stimulation. Either the amplitude or the latency of the response varies greatly on consecutive stimulations and there is also a remarkable tendency to habituation. Therefore, SSR is considered abnormal if no significant responses are detected. SSR is well correlated with other autonomic function tests, and its abnormality is documented in a variety of neurologic disorders such as diabetic neuropathy, cerebrovascular disease, and Parkinson's disease. In good methodological conditions, SSR is a simple, reliable indicator of sympathetic sudomotor outflow in central and PNS disorders.[5,6] Gamez-Nava *et al*. (2006) studied SSR produced by electrical stimuli in the same side of the body and notified that the latency for other side of the body was longer. The issue is due to single crossing over from a part of the body to the opposite part. This is a reason for supraspinal of the reflex pathway.[2] There have been many studies related to SSR done in patients with spinal cord injuries. Sanna G *et al*. (1992) in a study noted that the lack of SSR in people with spinal cord injury could be the result of anticholinergic drugs which inhibit SSR cholinergic mediators pathways.[3] In this study, 0.43 correlation was found between autonomy questionnaire scores and SSR. Shalimar G *et al*. (2004) reviewed neurophysiologic testing, correlation with clinical examination according to fiber type involvement and severity in sensory neuropathy and have concluded that the correlation between clinical examination and the results of an original neurophysiological test battery offers a comprehensive clinical and neurophysiological approach to the objective assessment of peripheral neuropathies according to fiber type involvement and overall severity.[12] Schestatsky P *et al*. (2000) studied SSR change in patients affected with Parkinson's disease and showed a significant decrease in average amplitude among these patients compared to control group.[13] The results of their study have been highlighted in the year 2006 by Borman P *et al*.[14] considering all the results of this study and many other studies, as the early recognition of abnormalities in ANS may be very important in order to prevent excessive morbidity, simple electrophysiological methods are suggested to identify SLE patients at high risk for symptomatic dysautonomia. It could be concluded that latency measures in SSR test can be used as a valuable and accurate evaluation guideline for autonomic system assessment. However, due to our small sample size, there is a need for more detailed studies with larger sample groups to support the results.

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Conflicts of interest
There are no conflicts of interest.

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