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Research Article

EVALUATION OF VASCULAR FUNCTION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Abstract: **Objective:** Systemic Lupus erythematosus (SLE) is an inflammatory autoimmune disease with multi organ involvement. Atherosclerosis occurs prematurely in SLE resulting in increased risk of cardiovascular morbidity and mortality. Arterial stiffness and endothelial dysfunction are the early events in the pathogenesis of atherosclerosis. Thus the aim of the study is to assess the arterial stiffness and endothelial dependent vasodilatation in SLE patients. **Methods:** Thirty six SLE patients and ten age matched healthy control subjects were recruited. Demographic data, associated risk factors, disease activity were collected. Vascular function was assessed noninvasively using PeriScope for arterial stiffness and Autodicrowin for reflection index. Unpaired student's't' test was used for statistical evaluation. **Results:** There was a significant arterial stiffness in both brachial ankle ($p<0.008$) and carotid femoral ($p<0.01$) pulse wave velocities. The change in reflection index was also significantly less ($p<0.0002$) from that of healthy controls. **Conclusion:** SLE patients had endothelial dysfunction and higher pulse wave velocities. Higher pulse wave velocities were found in longer disease duration patients.
Key**words:** Arterial stiffness, endothelial dysfunction, SLE

INTRODUCTION:

SLE is a connective tissue disease with wide spread organ involvement predominantly affecting females. Women with lupus in 35-44 years of age group were over 50 times more likely to have MI than women of similar age [1] and the risk of cardiovascular mortality and morbidity was high. Cardiovascular disease can not be entirely predicted by traditional risk factors [2] and atherosclerotic alterations in large arteries could make a significant contribution to the pathogenesis of cardiovascular disease. SLE related risk factors for atherosclerosis include systemic inflammation, autoantibodies to endothelium, HDL, phospholipids, circulating immune complexes, activated complement products, nephritis and dyslipidemia [3]. Increase in arterial stiffness is a marker of early vascular changes and development of atherosclerosis [4]. Pulse wave velocity (PWV) is a robust noninvasive method analyzing large artery elasticity and stiffness [5]. It is usually calculated based on pulse transit time and distance travelled between two points in arterial tree. Endothelial dysfunction (ED) is characterized by a reduction of the bioavailability of vasodilators in particular nitric oxide; where as endothelium-derived contracting factors are increased [6]. This imbalance leads to an impairment of endothelium dependent vasodilatation, which represents the functional characteristic of endothelial dysfunction. Reflection index, (height of diastolic to systolic multiplied by 100) is used as a marker for small artery tone.

MATERIALS & METHODS

Thirty six patients above 18 yrs of age diagnosed as SLE according to ACR criteria [7] were recruited after the protocol was approved by ethics committee. Age matched healthy control subjects (10) were recruited from relatives of patients. Subjects were excluded if they were pregnant or lactating or if they had cardiovascular or metabolic diseases. In patients, disease activity and damage index were assessed by SLEDAI [8] and damage index [9] respectively.

Assessment of Vascular Function

The study was conducted in the Clinical Pharmacology unit, NIMS, Hyderabad. Pulse Wave Velocity (PWV) & Reflection index (RI) was determined non-invasively by PeriScope [10] & Autodicrowin respectively Ms. Genesis Medical Systems, Hyderabad. The patients rested in supine position for 10 minutes before the recordings. RI was recorded at baseline and 15 min after 400 μgms of Salbutamol inhalation, the change in RI [11] was noted to assess the endothelial dependent vasodilatory function.

Statistical Analysis

The statistical analysis was performed using sigma graph pad software, USA version-4. All the data expressed as mean ± standard error of mean (SEM). The difference between two groups was determined by unpaired't' test. Spearman correlation was used to evaluate the associations between PWV, change in RI vs. duration of disease, SLEDAI, damage index. For statistical significance, the probability value of <0.05 was considered.

RESULTS

The study consists of 10 healthy controls and 36 SLE patients. The demographic data of patients and healthy controls is shown in table 1. There were no statistically significant differences between healthy controls and SLE

patients in relation to variables such as age, height, heart rate, blood pressure. In the patient group (31F, 5M) disease duration was 4 yrs. SLEDAI and damage index were 4 and 0 respectively. (Table 2*)*

Table 3 shows noninvasive assessments of vascular function in healthy controls and SLE patients. Brachial ankle (ba) PWV in SLE patients (1258 ± 29.97cm/s) was found significantly higher ($p< 0.008$) compared to healthy controls (1099 ± 18.68cm/s). Carotid femoral (CF) PWV in SLE patients (816 ± 24.91) was also high ($p <0.01$) compared to healthy controls. The change in RI in SLE patients (-1.89 ± 1.43) was significantly less ($p <0.0002$) from that of healthy controls (-13.58 ± 1.73).
Table 4 shows correlation coefficients between PWV, RI and the risk factors of cardiovascular disease in all SLE patients.

Table 1: Demographic data of patients and healthy controls

Parameter	Healthy controls	SLE patients
Age (yrs)	29.1 ± 2.62	32.81 ± 1.55
Height (cm)	158.8 ± 2.85	157.1 ± 1.32
Heart rate (beats/min)	76 ± 3.73	83 ± 1.73
Systolic blood pressure (mm of Hg)	117.7 ± 5.01	121.5 ± 3.28
Diastolic blood pressure (mm of Hg)	71 ± 1.93	78 ± 2.36
Mean arterial pressure (mm of Hg)	91.2 ± 2.52	97.2 ± 2.68
Pulse pressure (mm of Hg)	46.7 ± 3.71	43.4 ± 1.45

Data expressed as mean ± SEM

Table 2: Characteristics related to patients

Variable	Value
Women/ Men	31/5
Duration of disease	4.1 ± 0.6
SLEDAI	4.6 ± 1.1
Damage index	0.36 ± 0.1

Data expressed as mean ± SEM

Table 3: Mean Pulse Wave Velocities and Change in Reflection Index

Parameter	Healthy controls	SLE patients	p value
BAPWV (cm/s)	1099 ± 18.68	1258 ± 29.97	<0.008
CFPWV (cm/s)	695 ± 14.69	816 ± 24.91	<0.01
Change in RI	-13.58 ± 1.73	-1.89 ± 1.43	<0.0002

Data expressed as mean ± SEM

Table 4: Spearman correlation coefficient between PWVs, change in RI and the risk factors of cardiovascular disease in studied SLE patients

Parameter	BAPWV	CFPWV	Change in RI
Age	0.46 [a]	0.46 [a]	0.17
BMI	0.24	0.2	0.21
Duration of disease	0.348 [b]	0.386 [b]	-0.056
SLEDAI	0.017	0.017	0.041
Damage index	-0.176	-0.036	0.169
SBP	0.59 [c]	0.60 [c]	0.22
DBP	0.55 [c]	0.56 [c]	0.32
S. creatinine	0.05	0.05	-0.17
Total cholesterol	0.001	0.001	-0.14
HDL	0.18	0.18	-0.09
LDL	0.24	0.24	0.05
VLDL	0.34	0.38	0.05

[a] $p <0.005$, [b] $p < 0.05$, [c] $p <0.0005$

DISCUSSION

SLE is complicated by premature atherosclerosis and the pathogenesis is not clear. It may include the interactions between chronic inflammation, corticosteroid use, augmented traditional risk factors, kidney dysfunction and hypertension [12]. They contribute to alterations of the vasculature and the development of vascular stiffness and atherosclerosis.

PWV is a noninvasive method widely used as an index of large artery elasticity and stiffness [7]. In the present study, both the carotid femoral and brachial artery PWVs are higher in SLE patients when compared with the control group. Higher the velocity, higher the rigidity of the vascular wall and lower the distensibility. ED is believed to represent a widespread phenomenon that occurs at an early stage in the atherogenic process. The inflammatory process due to SLE as well as vascular thrombosis induced by antiphospholipid antibodies may contribute to ED. The decrease in RI from pre salbutamol to post salbutamol in SLE patients was significantly less from that of healthy controls, indicating impaired endothelial dependent vasodilatation in SLE patients.

Aging and environmental factors are responsible for structural and functional change of arterial wall, leading to decreased elasticity and increased stiffness. We found a significant correlation between age and pulse wave velocity both in brachial and carotid arteries. Selzer et al showed that traditional cardiovascular factors including age, blood pressure, and obesity are the risk factors associated with aortic stiffness measured by aortic PWV in postmenopausal SLE women [12]. The cause of raised blood pressure includes corticosteroid use, resulting weight gain kidney disease and potentially inflammation induced vascular injury. We also confirmed that age and blood pressure were significantly associated with increased PWV in patients with SLE.

The average disease duration of SLE in the present study is 4.1 yrs (range 0.3 – 20yrs) the duration of disease correlated significantly with PWV both in brachial and carotid artery, but not with RI suggesting large artery stiffness in patients with longer disease duration. SLEDAI and damage index did not correlate either with PWV or change in RI. SLE is a chronic disease characterized by exacerbations and remissions, thus measures of disease activity, damage index, laboratory assays and therapy vary with time

Several studies described a dyslipoproteinemia associated with active SLE that is characterized by increased triglycerides, VLDL cholesterol and reduced HDL cholesterol [13]. Higher levels of total cholesterol, triglyceride serum levels [14] are associated with increased risk for coronary artery disease. Though 11% of our patients had mild abnormalities in lipid profiles, significant correlation between total cholesterol, LDL, HDL levels and PWVs, change in RI was not observed. The lack of significant difference may be due to the small sample with each studied variable.

CONCLUSION

SLE patients had endothelial dysfunction and higher pulse wave velocities compared with age matched healthy controls. Higher pulse wave velocities were found in longer disease duration patients.

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