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## Respiratory Muscle Function and Spirometry in Patients with Systemic Lupus Erythematosus

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### ABSTRACT

**Background:** Systemic lupus erythematosus (SLE) can affect all organ systems including the respiratory tract and skeletal muscles. Some of the respiratory findings can be attributed to respiratory muscle involvement. The purpose of this study was to clarify the characteristics of pulmonary function tests (PFT), especially maximum inspiratory pressure (MIP) and maximum expiratory pressure (MEP) in females with systemic lupus erythematosus (SLE).

**Materials and Methods:** During a 12-month period, forced vital capacity (FVC), FEV<sub>1</sub>, FEF<sub>25-75</sub>, MIP, and MEP were measured prospectively in 76 consecutive female patients, suffering active SLE. The measured values were compared to an age-matched group of healthy women.

**Result:** FVC was lower in the patients than in controls (2.81 versus 3.64)  $P=0.000$ . Maximal inspiratory pressure (P<sub>I</sub>max) was lower in the female patients than in 78 controls (3.42 versus 7.36)  $P=0.000$ . Maximal expiratory pressure (P<sub>E</sub>max) was lower in the female patients than in controls (4.14 versus 9.68 kPa)  $P=0.000$ . There were no correlations between P<sub>I</sub>max or P<sub>E</sub>max and parameters of disease activity. Mouth occlusion pressure within the first 0.1 s of inspiration was higher in SLE patients than in controls (2.43 versus 1.38); however, the difference was not statistically significant ( $P=0.16$ ).

**Conclusion:** This study provides evidence of inspiratory and expiratory muscle weakness in SLE and may cause FVC reduction as well. The pathophysiologic mechanisms and the prognostic significance should be further investigated. (*Tanaffos* 2006; 5(4): 53-58)

**Key words:** Systemic lupus erythematosus, Pulmonary function tests, Maximum inspiratory pressure, Maximum expiratory pressure

### INTRODUCTION

Systemic lupus erythematosus (SLE) is an autoimmune disease that can affect most organ

systems. Respiratory involvement is a common feature in patients with SLE (1). The most common pulmonary complications are pleuritis, acute pneumonitis, chronic interstitial lung disease, muscular and/or diaphragm dysfunction, and alveolar haemorrhage (2,3). However, the use of more sensitive pulmonary function tests (PFT) can provide

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valuable information useful enough to detect subclinical pulmonary involvement (4). Pulmonary function test results in patients with SLE, including those with and without respiratory symptoms and abnormal chest roentgenograms, have frequently shown several abnormalities (5, 6, 7).

Martens et al. have suggested that; weakness of inspiratory and expiratory muscles may be the corresponding factor of restrictive ventilatory defects found in patients with SLE many years ago (8). With improvement of pulmonary muscle testing we decided to measure MIP and MEP in patients with SLE.

Several studies have attempted to correlate PFT with clinical and serological parameters of SLE with conflicting results. (9-11) The relatively small number of patients tested may have influenced the results of previous studies. In order to clarify the prevalence and features of PFT alterations, especially impairment of maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP), we prospectively assessed PFT in a number of patients with SLE.

## **MATERIALS AND METHODS**

During a 12-month period from June 2004 to December 2005 all of the female patients confirmed to suffer SLE in rheumatology clinic of Alzahra University Hospital (Isfahan), were referred to "Bamdad Respiratory Research Center"\* to undergo PFT including MIP and MEP measurements. Each patient had at least one of the active manifestations of SLE such as lupus nephritis, cutaneous manifestations, musculoskeletal involvement, pulmonary fibrosis, fever or haematological abnormalities. Patients with respiratory complaints (dyspnea, cough, hemoptysis) were excluded. Since only few men were observed during the study period, only females were included in the study.

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Seventy-six consecutive female patients, were selected. Their ages ranged from 16 to 69 years (mean±SD = 31.34±11.48). None of the patients had a history of current asthma, bronchitis, bronchiectasis, or noxious gas exposure. The mean duration of disease before admission was 3.5 years (range 3months-19years). All patients fulfilled the American Rheumatism Association (ARA) criteria for the diagnosis of SLE (12). During an initial evaluation, all patients underwent routine chest radiography. The presence of pulmonary fibrosis was determined by chest radiography, which revealed reticular or reticulonodular lesions, more prominent in the lung bases. A detailed physical examination and a routine clinical examination performed at the time of admission with special emphasis on signs and symptoms of other connective tissue diseases.

The following laboratory tests were evaluated: sodium, potassium, calcium, phosphorous, magnesium, anti-nuclear antibody (ANA), anti-dsDNA by enzyme immunoassay, hemoglobin, white blood cell, platelet, erythrocyte sedimentation rate, C3, C4, total hemolytic complement activity (CH50), and C-reactive protein (CRP). Clinical laboratory tests were performed according to standard hospital laboratory procedures.

All patients were on steroid therapy. Patients who underwent PFT and respiratory muscle function test before or within 2 weeks of the initiation or increase in dose of corticosteroid therapy were included.

### **Pulmonary and respiratory muscle function testing**

Spirometry was performed using body plethysmography machine (ZAN 500 body II), with the patient sitting, wearing a nose clip. The spirometers were calibrated daily with a built in calibration machine. Barometric pressures, measured daily by Isfahan airport, showed a range from 632 to 635 mm Hg. Room temperature was monitored using a Brooklyn NIST Centigrade thermometer and

kept 21 to 25 °C. Spirometry results were automatically corrected to BTPS conditions by spirometer software. Spirometry was performed in accordance with American Thoracic Society (ATS) guidelines by one technician. Spirograms were repeated until three acceptable tests were obtained or eight maneuvers. Studies were considered acceptable if the largest and second largest values for FVC and FEV<sub>1</sub> were within 200 ml of each other (13). If the first maneuvers were not satisfactory, further maneuvers were obtained until the reproducibility criteria were satisfied or 8 maneuvers were obtained. The instrument met the accuracy criteria of the ATS (14) and, as reported earlier, reproducibility criteria were met when the second largest FEV<sub>1</sub> and FVC were within 5% of the largest values. FEV<sub>1</sub>% predicted was calculated by dividing the observed FEV<sub>1</sub> by the corresponding predicted FEV<sub>1</sub> values.

In brief, P<sub>I</sub>max was determined during a deep inspiration from functional residual capacity against a shutter with a minor air leak preventing undesirable glottis closure. P<sub>E</sub>max was measured during maximal expiratory effort at total lung capacity. P<sub>I</sub>max and P<sub>E</sub>max were determined from the best of five consecutive maneuvers (varying <20%). A total of 2 min of rest was allowed between two maneuvers when necessary. Mouth occlusion pressure 0.1 s after the onset of inspiration (P<sub>0.1</sub>) was measured during spontaneous breathing at rest. P<sub>I</sub>max and P<sub>0.1</sub> are negative pressures with respect to atmosphere, but are expressed as positive values.

Spirometry results were compared with control normal values. Since published reference values for P<sub>I</sub>max, P<sub>E</sub>max and P<sub>0.1</sub> vary (15-16), values determined in 78 female healthy subjects served as controls.

Data analysis was performed using statistical package for the social sciences (SPSS, version 13).

All results are expressed as mean± SD. Unpaired t-tests were used to compare numeric values between cases and controls. A level of p<0.05 was accepted as statistically significant.

## RESULTS

FVC and FEV<sub>1</sub> and FEV<sub>1</sub>/FVC were lower in SLE patients than in controls (Table 1).

In SLE patients; Mouth occlusion pressures, P<sub>I</sub>max and P<sub>E</sub>max were significantly lower as compared with their respective controls. The reductions in P<sub>I</sub>max and P<sub>E</sub>max were independent from clinical data.

In SLE patients, mouth occlusion pressure within the first 0.1 second of inspiration (P<sub>0.1</sub>max) tended to be higher in SLE than in controls (2.43±6.39 versus 1.38±0.755); however, the increment did not reach statistical significance.

Table 1 lists the means ± SDs of the physical characteristics and physiologic data for the patients and control subjects. As can be seen, patients with systemic lupus erythematosus had functional values that were overall significantly less than corresponding values for the control subjects. In particular, FVC, FEV<sub>1</sub> were less, respectively, than corresponding control values.

**Table1.** Subject characteristic and pulmonary function

	Patients (n= 76 )	Controls (n= 78 )	P Value
Age(y)	31.34 ± 11.48	31.94± 12.05	0.75
Height(cm)	161.33±6.28	160.41±4.91	0.31
Female	76	78	
FVC	2.81	3.64	0.00
FEV <sub>1</sub>	2.35	3.16	0.00
FEV <sub>1</sub> /FVC	83.59	86.69	0.00
FEF <sub>25-75</sub>	2.65	3.71	0.00

P<sub>E</sub>max and P<sub>I</sub>max were also less, respectively, than their corresponding control values (table2).

**Table 2.** Maximal inspiratory ,expiratory and mouth pressure in 0.1second

	Patients	Control	Pvalue
MIP	3.42	7.36	0.00
MEP	4.14	9.68	0.00
P0.1	2.43	1.38	0.16

The primary clinical presentation on admission was cutaneous manifestation in 10 patients, renal disorder in 16, musculoskeletal involvement in 2, and fever in 3. Pulmonary disorders were infrequent (n = 4) as the major clinical manifestation. Raynaud's phenomenon was observed in 14 and renal disorder in 16 patients. Pulmonary fibrosis, determined by clinical and/or radiological evaluation, was not present but 8 patients had restrictive pulmonary function test in the absence of a clinical pulmonary disorder. Some patients tested positive for antibodies to dsDNA (n=57), ANA (n=62), anemia (n=26), elevated ESR (n=19), low C3 (n=14), low C4 (n=11), positive CRP (n=7), leukopenia (n=6), thrombocytopenia (n=6).

They had no electrolyte abnormalities.

The mean± SD values of MIP and MEP were 3.42±2.06 and 4.14±2.25, respectively. MIP and MEP were reduced in 16 patients.

MIP and MEP in patients correlated with FVC. No correlation was found between the impairment of MIP and MEP and the presence or absence of nephropathy and low complement level.

## DISCUSSION

There have been many studies concerning the characteristics of PFT in patients with SLE (5-7). We reported a reduction in diffusion lung capacity in patient with systemic lupus erythematosus (17). Therefore, we attempted to assess the characteristics of MIP and MEP and their correlation with clinical and immunological findings in patients with SLE.

The prevalence of impaired MIP and MEP in the present SLE patients is consistent with prior observations. Concerning the correlation between PFT alterations and disease activity, Silberstein et al. found no difference in clinical and immunological findings between SLE patients and those without PFT abnormalities (6). These discrepancies may be due to differences in the number of patients and the methods for evaluation of disease activity. In our study, reduction of MIP and MEP in SLE patients seems unlikely to correlate with disease activity.

The present study provides evidence of respiratory muscle dysfunction in SLE, as follows: 1) Both inspiratory and expiratory muscle strength (P<sub>I</sub>max and P<sub>E</sub>max) are reduced in patients with SLE as compared with respective controls; 2) Inspiratory and expiratory muscle weakness occurs independently from other clinical data.

In SLE, changes in P<sub>I</sub>max and P<sub>E</sub>max are independent of clinical parameters. In congestive left ventricular failure, the reduction in P<sub>I</sub>max exceeds the reduction in P<sub>E</sub>max, (18); whereas, in the present SLE patients, there is a close correlation between P<sub>I</sub>max and P<sub>E</sub>max. This is in concert with the parallel reduction in inspiratory and expiratory pressures seen in chronic obstructive pulmonary disease (COPD) patients (19).

The underlying mechanisms responsible for the respiratory muscle weakness in the present SLE patients are not known and were not the main focus of the present study.

Weakness of the respiratory muscles may be due to the pathologic changes in muscles, fatigue of muscles caused by overloading them, as well as impairments of the nervous system.

Electrolyte disturbances (20) and steroid therapy (21) have been identified to play a role in the development of inspiratory and expiratory muscle weakness. However, our SLE patients had no electrolyte status abnormality but were on steroid

therapy.

Activation of inspiratory muscles, including the diaphragm, is promoted by the ventilatory or central neural drive, which can be assessed indirectly by the measurement of P0.1. In our SLE patients, the increased P0.1/ PImax at rest indicates augmented ventilatory drive.

These results indicate that SLE patients may exhibit inspiratory muscle weakness and increase respiratory drive.

Steroid myopathy and myositis could explain the reduction in MIP whereas neural afferents arising from respiratory muscle, lung, or joint receptors could be involved in the observed increase in neural drive.

This study provides evidence of significant inspiratory and expiratory muscle weakness in SLE patients. The underlying mechanisms, response to treatment and potential role of prognostic markers of respiratory muscle dysfunction with SLE need further investigation.

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