Serial Pulmonary Function Testing in Patients with Systemic Lupus Erythematosus

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Previous studies have documented the pulmonary function abnormalities associated with systemic lupus erythematosus (SLE). There are very few data, however, regarding the progression of such changes. To study this question, we evaluated the pulmonary function of a group of 25 patients with SLE from two to seven years after a set of pulmonary function tests had been performed as part of their overall initial assessment. Reductions in diffusing capacity, FVC, and total lung capacity did not change significantly for the group over the period of our study. The mean FEF25–75%, which was initially low, and the mean FEV1/FVC ratio, which was initially normal, both decreased significantly. The observed abnormalities in airway function were not related to smoking history. Other aspects of lupus activity, as measured by serum creatinine levels and clinical activity, did not appear related to progression of lung disease.

Evaluation of pulmonary function in patients with systemic lupus erythematosus (SLE), including those with and without respiratory symptoms and abnormal chest roentgenograms, has shown a reduction in diffusing capacity in association with a restrictive pattern of lung disease. Histologic studies of the lungs of patients with SLE show changes that are consistent with observed physiologic changes. Abnormalities of pulmonary function at a single point in time do not correlate with other serologic or biopsy markers of SLE activity. Few data exist regarding the rate with which pulmonary function changes in patients with systemic lupus. To determine the degree to which pulmonary function might deteriorate over time in patients with SLE, we performed follow-up pulmonary function tests in a group of patients who had had pulmonary function testing done as part of their initial screening at an ambulatory lupus clinic at least two years earlier.

Materials and Methods

Randomly selected patients from the Lupus Clinic of Montefiore Medical Center, who as part of their overall initial assessment had pulmonary function testing, were restudied at least two years later. Twenty-five patients were ultimately restudied. All patients met four or more American Rheumatism Association requirements for diagnosis of SLE.

Pulmonary function testing included determination of static lung volumes, spirometric evaluation, and diffusion capacity. Lung volumes were calculated with a conventional water-sealed spirometer, and the functional residual capacity (FRC) was determined by the multiple-breath helium dilution technique. Spirometric measurements included FVC, FEV1, FEV1/FVC ratio, and the FEF25–75%. Measurement of the diffusing capacity of carbon monoxide was performed using the modified single-breath technique (Dsb) of Krogh.

The normal values of FVC, FEV1, and FEF25–75% were calculated from the prediction formulas of Morris et al. The normal values for the diffusing capacity were calculated from the equation given by Gaensler and Wright. Total lung capacity was calculated from the sum of the vital capacity and the residual volume, and normal values were taken from the work of Morris et al and Goldman and Becklake.

The FVC, FEV1, FEF25–75%, TLC, and Dsb were considered abnormal if they were less than 80 percent of the normal predicted value. The FEV1/FVC ratio was considered abnormal if less than 75 percent.

Pulmonary function studies (T1) were performed at least 24 months (mean, 58 ± 17 months) after the initial pulmonary evaluation (T0). All patients were stable without clinical evidence of acute pulmonary disease at the time of each study. The percent predicted values for FVC, FEF25–75%, TLC, Dsb, and FEV1/FVC ratio were compared for each subject at both test periods, except where noted in the Results section. The Wilcoxon signed rank test was used to statistically analyze individual changes in function between T0 and T1 for the overall group, as well as for nonsmokers and smokers.

Serum creatinine levels at T0 and T1 were compared for all patients. Changes in Dsb, TLC, FEV1/FVC, and FEF25–75% between T0 and T1 were compared with changes in serum creatinine using simple regression analysis. The clinical histories of all patients with a greater than 20 percent decrease in any parameter were reviewed between T0 and T1 in an attempt to correlate other aspects of lupus activity, including evidence of flares of arthritis, cerebritis, or vasculitis, to change in pulmonary function studies.

Results

Twenty-five patients were evaluated with serial pulmonary function studies. At the time of initial testing, the mean age of the group was 35 ± 13 years and ranged from 15 to 68 years. The mean interval of time separating pulmonary function studies was 56 ± 17 months and ranged from 24 to 84 months. Eight patients were cigarette smokers, and the mean pack-year smoking history for that group was 11 ± 6 pack-years. One patient, subject 4, had a past history...
of asthma but was stable and did not require treatment during the time of this study.

Table 1 shows mean pulmonary function data at T1 and T2. The initial pattern of function for the overall group was one of mild restriction with a mild reduction in Dsb. The initial mean FEF25–75% for the group was 75 ± 34 percent, with 12 of 25 subjects having values less than 80 percent of predicted. This reduction was present in both nonsmokers and smokers (Table 2). The FEV1/FVC ratio was initially normal for the group.

Changes in FVC, TLC, and Dsb between T1 and T2 were not significant (Wilcoxon signed rank test; p>0.05). The two measurements that showed significant decreases for the group overall were the FEV₁/FVC ratio and the FEF25–75% (Fig 1). Individual changes in the FEV₁/FVC ratio correlated well with the changes in FEF25–75% (r = 0.78; p<0.001). There was no significant correlation between changes in FVC and FEV₁/FVC or FEF25–75%. When the spirometric data were evaluated with respect to smoking history, only the decrease in FEV₁/FVC ratio in nonsmokers appeared significant (see Table 2). There was no correlation between the initial value of any function and the subsequent deterioration in that function.

The mean serum creatinine level, measured in mg/dl, increased significantly from 1.0 ± 0.3 SD at T1 to 1.2 ± 0.6 at T2. However, there were no correlations between individual reductions in any pulmonary function and increases in creatinine level. After chart review, there were no clinical signs of increased lupus activity that appeared to correlate with deterioration of pulmonary function.

<table>
<thead>
<tr>
<th>Table 1—Pulmonary Function Data at T1 and T2 (Mean ± SE)</th>
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<tbody>
<tr>
<td>Measurement</td>
</tr>
<tr>
<td>FVC, % pred</td>
</tr>
<tr>
<td>FEV1/FVC, %*</td>
</tr>
<tr>
<td>FEF25–75%, % pred†</td>
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<tr>
<td>TLC, % pred</td>
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<td>Dsb, % pred</td>
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*Mean at T1 significantly less than T2; p<0.02.
†Mean at T1 significantly less than T2; p<0.05.
Table 2—Smoking History and Spirometry (Mean ± SE)

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Non-smokers (N = 16)</th>
<th>Smokers (N = 9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV1/FVC, %</td>
<td>T1:82±3</td>
<td>T1:83±2</td>
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<tr>
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<td>T2:76±3*</td>
<td>T2:80±2</td>
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<tr>
<td>FEF25–75%, % pred</td>
<td>T1:74±9</td>
<td>T1:75±10</td>
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<tr>
<td></td>
<td>T2:61±10</td>
<td>T2:73±8</td>
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*Change at T2 from T1, significant, p<0.05.

DISCUSSION

Initial pulmonary function study results in our group of patients were typical of what is generally observed in SLE. Both mild restrictive and diffusion abnormalities were present. Neither the restrictive pattern of dysfunction nor the abnormality in diffusion demonstrated at initial testing progressed significantly for the overall group or for any of the subgroups. Initial levels of FVC, TLC, and Dsb did not appear to predict whether function would subsequently deteriorate. Lupus activity assessed over the time of study did not correlate with deterioration in pulmonary function.

The initial FEF25–75%, a reflection of small airway function, was reduced for the overall group and was unrelated to the smoking history or to the degree of restrictive pulmonary disease. Airway obstruction is not generally recognized to be a component of pulmonary dysfunction in SLE, although the data are conflicting.1,2,4,8,9,14,15 Specifically, with respect to the FEF25–75%, Chick et al16 failed to demonstrate significant reductions in this measure in their study of SLE. Marten et al,17 however, in a study addressing respiratory muscle dysfunction in SLE, showed values of FEF25–75% less than 60 percent of predicted in all seven of their patients. Collins et al18 measured the FEF25–75% in 17 patients with lupus and showed that six of 11 non-smokers had values less than 80 percent of predicted, with a mean of 61 percent.18 Pathologic changes, including peribronchial inflammation, emphysematous changes, and interstitial disease, are noted in several autopsy studies of patients with SLE and suggest an anatomic basis for small airway obstruction.5,6,19

Most interesting in our study was that the decreases in the FEV1/FVC ratio and in the FEF25–75% were significant over the time of study. These changes did not appear to be related to smoking history, although the smaller number of subjects in the smoking group makes analysis difficult. Changes in vital capacity were not related to flow changes. The lack of pathologic data demonstrating large airway involvement in SLE and the correlation between changes in the FEV1/FVC ratio and FEF25–75% suggest that the primary changes occurred at the level of the small airway. The etiology of these changes is unclear, but may reflect activity of the systemic disease. A more specific characterization is hampered, however, by the lack of widely accepted criteria to describe longitudinal lupus activity, the most accepted of which, changes in serum creatinine level, did not correlate with decreases in flow rate. Other less objective parameters of clinical activity also did not appear to relate to these changes.

The pulmonary function abnormalities we demonstrated in this study of SLE are consistent with prior observations, but also point out a significant incidence of airway obstruction involving primarily the small airways. These may be progressive and suggest continued pulmonary inflammation related to lupus activity or possibly subclinical infection. Continued long-term studies along with greater availability of lung biopsy material should help to further characterize these abnormalities.

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REFERENCES

NIOSH Spirometry Course

Practical Spirometry Course. Two day, hands-on, NIOSH approved course for certification in pulmonary function testing will be presented by the Mayo Clinic Pulmonary Services. The courses in 1988 will be held August 17-18 in Monterey, California, and October 19-20 in Quechee, Vermont. Approved by AAOHN for 17.7 contact hours. For further details call 800/533-1653.