Lupus-associated pulmonary hypertension: Long-term response to vasoactive therapy

Gustavo A. Heresi, Omar A. Minai*

Department of Pulmonary, Allergy, and Critical Care Medicine, Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, OH 44195, USA

Received 12 February 2007; accepted 25 May 2007
Available online 6 July 2007

Summary

Introduction: Pulmonary hypertension (PH) is a serious complication of lupus. The effectiveness of current vasoactive therapy has not been well described.

Methods: Retrospective analysis of 12 patients with lupus-associated PH (age 43 ± 10 years, mean ± SD, all female) treated with pulmonary vasodilators.

Results: At baseline, patients had severe PH: median six-minute walk distance (6MWD) 266 m (95% confidence interval [CI], 106 to 362); functional class III (n = 7) and IV (n = 5); mean pulmonary artery pressure (mPAP) 52 mmHg and cardiac index 2.23 L/min/m². Eight patients were started on epoprostenol and 2 each on bosentan or treprostinil. After a mean follow-up of 41 ± 25 months, 5 patients were on combination therapy (3 epoprostenol plus bosentan, 1 treprostinil plus bosentan, 1 bosentan plus sildenafil) and 7 were on monotherapy (2 epoprostenol, 4 bosentan, 1 sildenafil); 6MWD increased by 139 m (95% CI, 36 to 259, p = 0.007), 8 patients were functional class I or II and 4 were class III; right ventricular systolic pressure (RVSP) decreased by 22 mmHg (95% CI, 6 to 36; p = 0.012), mPAP decreased by 18 mmHg (95% CI, 8 to 29; p = 0.014), and cardiac index increased by 1.44 L/min/m² (95% CI, 0.76 to 2.08; p = 0.016). There was no mortality or need for lung transplantation. Therapy was well tolerated.

Conclusions: Vasoactive therapy can achieve sustained clinical and hemodynamic improvement in lupus-associated PH.

© 2007 Elsevier Ltd. All rights reserved.
Introduction

Pulmonary hypertension (PH) is a well-recognized complication of collagen vascular diseases. This association is better appreciated for patients with the scleroderma spectrum of disease, and less so for patients with systemic lupus erythematosus (SLE). The prevalence of PH in patients with SLE has varied in different series most likely as a result of increasing awareness, wider access to better noninvasive measurements of right ventricular systolic pressure (RVSP), and differences in the way PH has been defined. In a recent study, using a cutoff of 40 mmHg for RVSP measured by Doppler echocardiography, Johnson et al. found a prevalence of 14% in a cohort of 129 patients with SLE, similar to estimates in systemic sclerosis. Thus, SLE-associated PH appears to be more common than previously recognized. The etiology of PH in patients with SLE is multi-factorial and arteriopathy involving the pulmonary vasculature, with increasing pulmonary vascular resistance and vasoconstriction, is felt to play a role. However, therapeutic decisions remain guided by scant literature comprised of case reports or small case series. Several studies have suggested a guarded prognosis for SLE-associated PH, with substantial mortality. These data precede the introduction of selective pulmonary vasodilators.

We describe a single center series of 12 patients with SLE-associated PH treated with parenteral and oral vasoactive agents, with a focus on long-term outcomes.

Methods

The study was approved by our Institutional Review Board. Medical records of patients followed in the PH clinic at the Cleveland Clinic were retrospectively reviewed to identify patients who met the revised American Rheumatism Association diagnostic criteria for SLE. All patients had undergone a work-up to rule out other causes of PH as recommended by current guidelines.

Medical records were analyzed for clinical parameters, laboratory testing, 6-min walk test, echocardiographic, and right heart catheterization (RHC) data at baseline, 3 and 6 months, 1, 2 and 3 years after initiation of vasodilator therapy and at last follow-up.

Data at individual time points are presented as means and 95% confidence intervals (CI) based on the T distribution. For each variable, the last follow-up value was defined as the most recent available value. Absolute change from baseline to follow-up was also described using the mean and a 95% CI. Each variable is summarized at individual time points using all available data, but comparison of a follow-up time point to baseline uses only patients with data at both follow-up and baseline in a paired fashion. For the 6-min walk distance (6MWD), we assigned a result of 0 m at baseline to patients who were admitted to the hospital with symptoms of overt right-sided heart failure for emergent initiation of vasodilator therapy and were unable to perform the test. We used medians and CI based on signed-rank tests to describe the walk distances at individual time points, as well as change from baseline. The Wilcoxon signed-rank test was used to assess the statistical significance of changes from baseline to follow-up, and to produce the corresponding CI. R version 1.9.0 was used to perform the tests.

Results

Baseline characteristics are shown in Table 1. All cases were women, with a mean age of 43 ± 10 years. Mean time since diagnosis of SLE to the diagnosis of PH was 9.25 years. At the time of the diagnosis of PH, 10 patients were on immunosuppressive therapy, most commonly prednisone or hydroxychloroquine. During the study period 9 patients were on warfarin therapy. Three patients (#2, 6 and 10) had a lupus flare during the study period, and in 1 patient (#10) an SLE flare occurred shortly before the diagnosis of PH was made. Pulmonary function testing results were available for 10 patients. Flows and volumes were normal in 7 and showed moderate restriction (n = 1), mild obstruction (n = 1), or severe obstruction with restriction (n = 1) in the others. Carbon monoxide diffusion capacity (DLCO) was available in 6 patients and was moderately (n = 2) or severely (n = 3) reduced in the majority. Interestingly, the 3 patients with intermediate or high probability ventilation perfusion scans had negative pulmonary angiograms for pulmonary embolism.

Table 2 outlines clinical, hemodynamic and treatment characteristics of the patients. At baseline, 7 patients had New York Heart Association (NYHA) class III and 5 had class IV symptoms, and median 6MWD was 266 m (95% CI, 106 to 362). Four patients were in overt right-heart failure and unable to perform the 6-min walk. Mean RVSP estimated by Doppler echocardiography was 77 mmHg (95% CI, 65 to 88). All patients had evidence of right ventricular dilation, but no pericardial effusions were detected by echocardiography. Baseline RHC information was available for all patients. One patient (#3) was diagnosed with PH during a pulmonary angiogram and refused RHC. Mean right atrial pressure was 12 mmHg (95% CI, 7 to 18), mean pulmonary artery pressure (mPAP) was 52 mmHg (95% CI, 46 to 58), and cardiac index was 2.23 L/min/m² (95% CI, 1.89 to 2.57).

Eight patients were started on epoprostenol, 2 on subcutaneous treprostinil, and 2 on bosentan. Mean follow-up was 41 ± 25 months (mean ± SD). Most patients demonstrated an impressive response to therapy (Table 2, Figs. 1–3). After 3 months, 6MWD increased by a median of 57 m (95% CI, 7 to 235, p = 0.04) and 10 patients had improved by at least one NYHA functional class.

At last follow-up, 8 patients were NYHA class I or II and 4 were NYHA class III (Fig. 1). Four patients were on combination therapy including a parenteral prostacyclin (3 on epoprostenol plus bosentan, and 1 on subcutaneous treprostinil plus bosentan), 1 patient was on bosentan plus sildenafil, and 7 patients were on single-drug therapy (2 on epoprostenol, 4 on bosentan and 1 on sildenafil). Compared to baseline, 6MWD increased by a median of 139 m (95% CI, 36 to 259; p = 0.007). When analyzing only those patients who had a baseline 6MWD (n = 8), the improvement to last follow-up was a median of 55 m (95% CI, −9 to 134, p = 0.11). RVSP decreased by a median of 22 mmHg (95% CI, 6 to 36; p = 0.012), mPAP decreased by 18 mmHg (95% CI,
8 to 29; \( p = 0.014 \), and cardiac index increased by 1.44 L/min/m² (95% CI, 0.76 to 2.08; \( p = 0.016 \)) (Fig. 2). Repeat RHC data were not available in all patients, as depicted in Fig. 2, but where available (\( n = 8 \) for mPAP, \( n = 7 \) for cardiac index), it showed a decrease in mPAP and an increase in cardiac index. Three patients (see Table 2) were transitioned from a parenteral prostacyclin to oral therapy (2 to bosentan and 1 to bosentan plus sildenafil) and

<table>
<thead>
<tr>
<th>Pt</th>
<th>Age (years)</th>
<th>Raynaud’s</th>
<th>Positive antibodies</th>
<th>SLE medications</th>
<th>( T_1 ) (years)</th>
<th>Presenting symptoms</th>
<th>Chest CT</th>
<th>VQ scan</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>29</td>
<td>No</td>
<td>ANA and ds-DNA</td>
<td>Hydroxychloroquine</td>
<td>0</td>
<td>Syncope</td>
<td>Normal parenchyma</td>
<td>Low probability</td>
</tr>
<tr>
<td>2</td>
<td>37</td>
<td>Yes</td>
<td>ANA, ds-DNA, Smith and RNP</td>
<td>Prednisone and hydroxychloroquine</td>
<td>6</td>
<td>Dyspnea</td>
<td>Normal parenchyma</td>
<td>Large symmetric mismatched defects in both upper lobes, PA gram showed no filling defects</td>
</tr>
<tr>
<td>3</td>
<td>53</td>
<td>No</td>
<td>ANA</td>
<td>Prednisone, hydroxychloroquine and methotrexate</td>
<td>24</td>
<td>Dyspnea and syncope</td>
<td>Normal parenchyma</td>
<td>Low probability</td>
</tr>
<tr>
<td>4</td>
<td>49</td>
<td>NA</td>
<td>ANA</td>
<td>Prednisone and hydroxychloroquine</td>
<td>15</td>
<td>Dyspnea</td>
<td>Bilateral lower lobes interstitial infiltrates; mild pericardial thickening</td>
<td>Low probability</td>
</tr>
<tr>
<td>5</td>
<td>42</td>
<td>No</td>
<td>ANA, anti-phospholipid and RNP</td>
<td>Prednisone</td>
<td>2</td>
<td>Dyspnea</td>
<td>Normal</td>
<td>NA. PA gram negative for PE</td>
</tr>
<tr>
<td>6</td>
<td>40</td>
<td>Yes</td>
<td>ANA, ds-DNA, Smith and RNP</td>
<td>Prednisone and cyclophosphamide, methotrexate (discontinued)</td>
<td>3</td>
<td>Dyspnea</td>
<td>Scattered small patchy infiltrates, small bilat pleural effusions, small pericardial effusion</td>
<td>NA</td>
</tr>
<tr>
<td>7</td>
<td>56</td>
<td>Yes</td>
<td>ANA, ds-DNA, Smith</td>
<td>Hydroxychloroquine</td>
<td>20</td>
<td>Dyspnea</td>
<td>Normal. No PE</td>
<td>NA</td>
</tr>
<tr>
<td>8</td>
<td>46</td>
<td>Yes</td>
<td>NA</td>
<td>None (previously on prednisone, cyclophosphamide and hydroxychloroquine)</td>
<td>14</td>
<td>Dyspnea, chest pain and syncope</td>
<td>Sub-segmental atelectasis RML, RLL pleural thickening</td>
<td>Intermediate probability. PA gram negative for PE</td>
</tr>
<tr>
<td>9</td>
<td>61</td>
<td>Yes</td>
<td>ANA, ds-DNA, IgM cardiolipin</td>
<td>None</td>
<td>0</td>
<td>Dyspnea</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>10</td>
<td>38</td>
<td>NA</td>
<td>ANA, ds-DNA, IgM cardiolipin, lupus AC and RNP</td>
<td>None</td>
<td>8</td>
<td>Dyspnea</td>
<td>Scattered hazy opacities bilaterally, otherwise normal</td>
<td>Low probability</td>
</tr>
<tr>
<td>11</td>
<td>34</td>
<td>Yes</td>
<td>ANA, ds-DNA, Smith, IgG cardiolipin, lupus AC and RNP</td>
<td>Prednisone, hydroxychloroquine and mycophenolate motefil</td>
<td>14</td>
<td>Dyspnea</td>
<td>Minimal bilateral basilar atelectasis and fibrosis</td>
<td>High probability, but PA gram negative for PE</td>
</tr>
<tr>
<td>12</td>
<td>30</td>
<td>No</td>
<td>ANA, ds-DNA</td>
<td>Hydroxychloroquine and mycophenolate motefil</td>
<td>5</td>
<td>Dyspnea</td>
<td>Vague patchy RLL alveolar infiltrate, pericardial effusion. No PE</td>
<td>NA</td>
</tr>
</tbody>
</table>

**Table 1** Baseline clinical features of 12 patients with lupus-associated pulmonary hypertension.

**Abbreviations:** Pt, patient; SLE, systemic lupus erythematosus; \( T_1 \), time from diagnosis of SLE to diagnosis of pulmonary hypertension; CT, computed tomography; VQ, ventilation-perfusion; ANA, antinuclear antibodies; ds-DNA, double-stranded deoxyribonucleic acid; RNP, ribonucleoprotein; RML, right middle lobe; RLL, right lower lobe; PA gram, pulmonary angiogram; PE, pulmonary embolism; NA, not available.
<table>
<thead>
<tr>
<th>Pt</th>
<th>NYHA</th>
<th>6MWD (m)</th>
<th>RHC (RAP, mPAP, CI, PCWP, PVR)</th>
<th>PH medications</th>
<th>Duration of each therapy</th>
<th>Follow-up in months</th>
<th>6MWD (m)</th>
<th>RHC (RA, mPAP, CI, PCWP, PVR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>III</td>
<td>454</td>
<td>2</td>
<td>Treprostinil+bosentan</td>
<td>11 months+9 months</td>
<td>11</td>
<td>588</td>
<td>NA</td>
</tr>
<tr>
<td>2</td>
<td>III</td>
<td>354</td>
<td>14</td>
<td>Epoprostenol+bosentan</td>
<td>42 months+33 months</td>
<td>42</td>
<td>444</td>
<td>NA</td>
</tr>
<tr>
<td>3</td>
<td>III</td>
<td>473</td>
<td>7</td>
<td>Treprostinil (discontinued); bosentan</td>
<td>20 months; 27 months</td>
<td>56</td>
<td>525</td>
<td>3</td>
</tr>
<tr>
<td>4</td>
<td>III</td>
<td>319</td>
<td>9</td>
<td>Epoprostenol</td>
<td>46 months</td>
<td>46</td>
<td>518</td>
<td>8</td>
</tr>
<tr>
<td>5</td>
<td>III</td>
<td>288</td>
<td>NA</td>
<td>Bosentan</td>
<td>21 months</td>
<td>18</td>
<td>270</td>
<td>10</td>
</tr>
<tr>
<td>6</td>
<td>IV</td>
<td>0</td>
<td>26</td>
<td>Epoprostenol</td>
<td>81 months</td>
<td>81</td>
<td>447</td>
<td>6</td>
</tr>
<tr>
<td>7</td>
<td>IV</td>
<td>0</td>
<td>8</td>
<td>Epoprostenol+bosentan</td>
<td>106 months+36 months</td>
<td>82</td>
<td>355</td>
<td>10</td>
</tr>
<tr>
<td>Case</td>
<td>NYHA</td>
<td>Age (yrs)</td>
<td>Event</td>
<td>Epoprostenol (discontinued); sildenafil</td>
<td>6MWD (m)</td>
<td>6MWD (m)</td>
<td>RVSP (mmHg)</td>
<td>RAP (mmHg)</td>
</tr>
<tr>
<td>------</td>
<td>------</td>
<td>-----------</td>
<td>-------</td>
<td>----------------------------------------</td>
<td>----------</td>
<td>----------</td>
<td>-------------</td>
<td>------------</td>
</tr>
<tr>
<td>8</td>
<td>III</td>
<td>244</td>
<td>24</td>
<td>Epoprostenol (discontinued); sildenafil</td>
<td>3 months; 20 days</td>
<td>3</td>
<td>261</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>50</td>
<td>1.8</td>
<td>12</td>
<td>10</td>
</tr>
<tr>
<td>9</td>
<td>IV</td>
<td>212</td>
<td>6</td>
<td>Treprostinil (discontinued); epoprostenol+bosentan</td>
<td>1 months; 52 months+30 months</td>
<td>52</td>
<td>236</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>47</td>
<td>3.0</td>
<td>10</td>
<td>6</td>
</tr>
<tr>
<td>10</td>
<td>IV</td>
<td>0</td>
<td>NA</td>
<td>Epoprostenol (discontinued); bosentan+sildenafil</td>
<td>9 months; 25 months+24 months</td>
<td>34</td>
<td>162</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>48</td>
<td>1.7</td>
<td>10</td>
<td>11</td>
</tr>
<tr>
<td>11</td>
<td>III</td>
<td>404</td>
<td>16</td>
<td>Epoprostenol (discontinued); bosentan</td>
<td>36 months; 29 months</td>
<td>41</td>
<td>370</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>65</td>
<td>2.4</td>
<td>14</td>
<td>9</td>
</tr>
<tr>
<td>12</td>
<td>III</td>
<td>0</td>
<td>12</td>
<td>Bosentan</td>
<td>19 months</td>
<td>19</td>
<td>363</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>50</td>
<td>2.7</td>
<td>11</td>
<td>10</td>
</tr>
</tbody>
</table>

**Abbreviations:** NYHA, New York Heart Association; 6MWD, 6-min walk distance; TTE, transthoracic echocardiogram; RVSP, right ventricular systolic pressure (mmHg); RHC, right heart catheterization; RAP, right atrial pressure (mmHg); mPAP, mean pulmonary artery pressure (mmHg); CI, cardiac index (L/min/m²); PCWP, pulmonary capillary wedge pressure; PVR, pulmonary vascular resistance (Woods units); PH, pulmonary hypertension; NA, not available.

*Last follow-up adjusted to the six-minute walk distance.

1Baseline.

2Last follow-up.

3Timing of repeat RHC was variable; it occurred on average 17.5 months after baseline (range, 2–60 months).

4Transitioned from parenteral prostacyclin to oral therapy.
Figure 1  New York Heart Association functional class at baseline and throughout follow-up. Abbreviation: NYHA, New York Heart Association.

Figure 2  Change in 6-min walk distance, right ventricular systolic pressure, mean pulmonary artery pressure, and cardiac index from baseline to last follow-up (mean 41 months). Follow-up mean pulmonary artery pressure and cardiac index occurred on average 17.5 months after baseline (range, 2–60 months). The lateral diamonds and bars represent the medians and 95% confidence intervals (CI) for the 6-min walk distance and means and 95% CI for the other parameters.

Figure 3  Change in 6-min walk distance and right ventricular systolic pressure over time. Data presented as medians and 95% confidence intervals (CI) for the 6-min walk distance and means and 95% CI for the right ventricular systolic pressure. Abbreviations: 6-MWD, 6-min walk distance; RVSP, right ventricular systolic pressure.
showed continued benefit after a mean follow-up of 26.7 months. Thus, vasoactive therapy accomplished early and sustained clinical and hemodynamic beneficials in this group of patients, as depicted in Fig. 3 regarding 6MWD and RVSP.

There was no mortality during the follow-up time and no patient needed to undergo lung transplantation. One patient (#8) on epoprostenol developed severe thrombocytopenia and a skin rash that resolved after discontinuation of the drug and transition to oral bosentan and sildenafil. There were no cases of abnormal liver function tests with bosentan. Otherwise, side effects were typical of the known drugs’ profiles.

Discussion

We describe a series of patients with SLE-associated PH treated with parenteral and oral vasoactive agents. Our patients had severe SLE-associated PH and demonstrated clinical and hemodynamic benefits as early as 3 months after the initiation of therapy, which were sustained over a mean follow-up of 41 months. This is the largest series to show that benefits obtained initially with parenteral and oral vasoactive agents, can be sustained long-term in patients with SLE-associated PH.

Time between diagnosis of SLE and PH was variable, was not necessarily related to disease activity, and PH was the presenting feature leading to a diagnosis of SLE in 2 patients. Presenting symptoms and signs in our patients were non-specific.

Few studies have reported pulmonary function test results in these patients. One report found normal flows and volumes with a moderately decreased DLCO. Most of our patients had normal flows and volumes; however, when available, the DLCO was usually abnormal. Larger studies in patients with SLE with and without PH are required to better delineate the significance of this finding, and whether this can be used as an early indicator of a high likelihood of PH, similar to patients with scleroderma. Some authors have attempted to divide patients with PH and SLE into primary and secondary PH, i.e., those without and with significant pulmonary or left-sided cardiac disease, respectively. Only one of our patients (#3) had significant interstitial lung disease with moderate to severe restriction and may be characterized as secondary PH, and none had significant left-sided cardiac disease. The lack of left-sided heart disease, pulmonary emboli and interstitial lung disease indicates that these patients were symptomatic from pulmonary vascular involvement due to SLE.

Echocardiography was performed serially in all of our patients. Transthoracic echocardiography can be relatively accurate in predicting pulmonary arterial pressure in this patient population. However, the shortcomings of Doppler measurement of pulmonary artery systolic pressure are well recognized. In view of the dearth of information about the extent of hemodynamic abnormalities and how these relate to baseline characteristics and response to therapy in patients with SLE-associated PH, it is our recommendation that all patients with SLE suspected to have PH should undergo RHC prior to initiation of therapy.

PH in the setting of collagen vascular disorders is commonly associated with a poor prognosis. This has been shown by data mainly from patients with PH associated with scleroderma. It is also recognized that patients with scleroderma have a significantly worse prognosis if they develop PH. Data in patients with SLE-associated PH are scant and suggest that PH in the setting of SLE carries a poor prognosis. However, these data predate the use of modern pulmonary vasoactive therapy.

Multi-center trials have led to the approval of parenteral, inhaled, and oral vasoactive agents that act as pulmonary vasodilators and may also possess anti-thrombotic, anti-fibrotic and anti-mitogenic properties. Recent evidence suggests that patients with PH may obtain sustained benefit with the use of monotherapy or combination therapy in the appropriate clinical setting. In our series, patients had a significant response to parenteral and/or oral vasodilators with improved functional parameters and hemodynamics. Recently, Chung et al. found a significantly worse survival in 20 patients with SLE-associated PH compared to 34 with idiopathic PH (3- and 5-year survival rates of 45% and 17% vs. 73% and 68%, respectively). However, only 11 SLE-PH patients (55%) were treated with a vasoactive agent, namely beraprost, which has been shown to be ineffective long-term in patients with PH. In addition, only 3 patients were on warfarin therapy, and half of the SLE patients did not receive a RHC to confirm the diagnosis. In our series there was no mortality after a mean follow-up of 41 months, no patient required lung transplantation and 3 patients were transitioned from parenteral prostacyclin to oral therapy with continued improvement. These findings, coupled with the significant clinical and hemodynamic response observed, suggest that, if appropriately treated with current pulmonary vasodilator therapy, this patient population may have a better prognosis than previously recognized.

This kind of clinical and hemodynamic response has been previously reported. Robbins et al. described a series of 6 patients with SLE-associated PH treated with continuous intravenous epoprostenol. Baseline clinical and hemodynamic features were remarkably similar to the subjects in our series, as was the magnitude of both the clinical and hemodynamic response.

Therapy was well tolerated in our series. Only 1 patient developed thrombocytopenia felt to be related to epoprostenol, which resolved upon discontinuation of the drug. Close monitoring is warranted though, since life-threatening thrombocytopenia in SLE patients treated with epoprostenol has been reported.

Only 3 patients experienced a lupus exacerbation during the course of follow-up. There are reports of improvement in SLE-associated PH with immunosuppressive therapy. However, other reports suggest poor or no response. Benefit has also been reported when treating with a combination of vasodilators and immunosuppressive agents. Most of our patients were on stable doses of immunosuppressants or were treated with increasing doses for a short period of time, without appreciable changes in their PH. It is clear from our series that patients with SLE-associated PH have a favorable short- and long-term response to vasoactive therapy with both parenteral and oral agents and, until larger studies are performed, these
should probably be the first-line therapy for such patients. The role of immunosuppressive agents either alone or in combination with vasoactive agents requires further study.

This report has the limitations of any retrospective case series. We did not have a control population and not all patients had follow-up RHC. Treatment was heterogeneous; however, we decided to include all patients to draw attention to the fact that patients had an excellent response to both parenteral and oral agents of different classes and that benefit was sustained despite the necessity to change therapies in some patients. Reports like this can provide information about current clinical practice and can guide the design of prospective, controlled, randomized trials.

In conclusion, we present a series of patients with SLE-associated PH who showed improvement in their clinical and hemodynamic parameters with the use of pulmonary vasodilators. This improvement was sustained over a mean follow-up of 41 months. These findings suggest that, if appropriately diagnosed and treated, these patients may have a better prognosis than previously suspected, especially in the era of modern vasoactive therapy. Prospective randomized trials of vasoactive agents specifically for patients with SLE-associated PH are warranted.

Conflict of interest

- Gustavo A. Heresi has no relationships with pharmaceutical companies, biomedical device manufacturers or other corporations whose products or services are related to the subject matter of the article.
- Omar A. Minai has served in the Speakers’ Bureau and received honoraria from Actelion, United Therapeutics and Pfizer. He has been a consultant for Actelion, United Therapeutics, Myogen and Encysive.

References