Primary Pulmonary Hypertension Treated with Short-Term Epoprostenol Infusion

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Abstract

We describe the use of short-term epoprostenol in a 61-year-old man with primary pulmonary hypertension. The patient was on a ventilator because of respiratory distress. Continuous infusion of epoprostenol was started and it initially reduced the pulmonary artery pressure by 32%. Epoprostenol was tapered, and even after discontinuation, the pulmonary artery pressure was controlled. The ventilator was removed, and the patient remained well on home oxygen therapy 3 months after discharge. (Internal Medicine 42: 824-826, 2003)

Key words: epoprostenol, pulmonary artery pressure, primary pulmonary hypertension

Introduction

Primary pulmonary hypertension (PPH) is a progressive disease characterized by increased pulmonary vascular resistance, which leads to right ventricular failure. The mean survival from its onset is estimated to be about 3 years (1). Various therapeutic approaches have been advocated for PPH, such as vasodilators, anticoagulation, and heart-lung transplantation. Recently, continuous infusion of prostacyclin has been introduced for the treatment of PPH, and this has improved long-term survival. However, there is no consensus regarding dosing strategies of epoprostenol, and the mechanism of its beneficial effects remains unknown (2). We attempted short-term epoprostenol in a patient with PPH who responded well to this therapy. We report this case with a review of the literature.

Case Report

A 61-year-old Japanese man with PPH requiring high-flow supplemental oxygen for 8 years, Parkinson’s syndrome for 13 years, and a history of subarachnoid hemorrhage was admitted because of progressive dyspnea on exertion. Primary pulmonary hypertension was diagnosed at another hospital 8 years previously, when the patient underwent right heart catheterization to exclude congenital or acquired heart disease. This procedure indicated pulmonary artery pressure of 54/26 mmHg, mean pulmonary capillary wedge pressure of 4 mmHg, right ventricular pressure of 57/4 mmHg, and right atrial pressure of 3 mmHg. Cardiac output was 3.3 l/min, and right-to-left shunting was 0.8 l/min. Pulmonary angiography showed normal findings. A lung perfusion scan detected no evidence of pulmonary thromboembolic disease. An echocardiogram indicated the presence of pulmonary hypertension, right atrial and ventricular enlargement, and an interatrial septum aneurysm with a right-to-left shunt via a patent foramen ovale. Evaluation excluded causes of secondary pulmonary hypertension including congenital or acquired heart diseases, respiratory system disorders, and collagen vascular diseases. In this case atrial septal defect with Eisenmenger syndrome was unlikely given the relatively small shunt ratio, the acute onset of symptoms, and the absence of characteristic features or physiologic findings of atrial septal defect in childhood. The patient thus fulfilled the criteria of the National Institutes of Health Registry on Primary Pulmonary Hypertension (3). He had been treated with alacepril, furosemide, warfarin, beraprost (an orally active prostacyclin analogue), and high-flow supplemental oxygen. He also suffered from Parkinson’s syndrome and was treated with the dopamine receptor agonist, L-dopa, an aromatic amino acid decarboxylase inhibitor, and a muscarinic antagonist.

Physical examination revealed a middle-aged man in respiratory distress. Temperature was 36.5°C, BP was 126/90 mmHg, pulse was 74 beats/min, and respiration was 24 breaths/min. Cardiac auscultation revealed a loud S2 and a grade 3/6 systolic murmur over the left lower sternal border. Auscultation of the lungs revealed normal vesicular sounds.
Neurologic examination revealed slight rigidity of both upper arms, gait disturbance, dysarthria, and slight disorientation. Laboratory data on admission were unremarkable except for severe hypoxemia. Arterial blood gas analysis while the patient was breathing oxygen 7 l/min by face mask revealed the following: pH 7.44; PaCO2 23.8 mmHg; PaO2 55.0 mmHg; and oxygen saturation 90.5%. An initial sputum culture yielded normal flora and a sputum stain for acid-fast bacteria was negative. Chest roentgenogram showed prominent pulmonary arteries with clear lung fields (Fig. 1).

The patient underwent endotracheal incubation 6 hours after admission because of deteriorating blood gases and increasing respiratory distress. The patient remained in poor condition over the next 12 hours, requiring positive end-expiratory pressure of 3 cm H2O and a 100% fraction of inspired oxygen to maintain an oxygen saturation of 95%. An initial hemodynamic study showed a mean pulmonary arterial pressure and total pulmonary resistance of 82 mmHg and 2,260 dyne s cm⁻⁵, respectively. Cardiac output was 2.9 l/min.

On the third hospital day, a continuous intravenous infusion of epoprostenol was started at 0.5 ng/kg/min and then increased gradually to 5 ng/kg/min. Mean pulmonary pressure and total pulmonary resistance were reduced by 32.9% and 47.4%, respectively. Cardiac output increased by 27.6%. His condition improved, and the ventilator was removed on the 30th hospital day.

Treatment with epoprostenol was carried out for a total of 24 days, with the dose reduced by 1 ng/kg/min every 1 or 2 days after the first 17. Hemodynamic measurements obtained 2 days after discontinuation of epoprostenol demonstrated a continued reduction in pulmonary vascular resistance in association with an increase in cardiac index; the pulmonary artery pressure was 52/24 mmHg, cardiac output 3.7 l/min, and total pulmonary resistance 799 dyne s cm⁻⁵ (Table 1). The patient's course continued to improve, and he was discharged on the 91st hospital day. No calcium channel blockers were ever used because of low systemic blood pressure. Blood gas analysis at discharge revealed pH 7.5.

### Table 1. Hemodynamic Variables at Baseline, during and after Intravenous Epoprostenol Therapy

<table>
<thead>
<tr>
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<th>Baseline</th>
<th>During epoprostenol therapy</th>
<th>Two days after discontinuation of epoprostenol</th>
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<tbody>
<tr>
<td>Heart rate (beat/min)</td>
<td>86</td>
<td>91</td>
<td>97</td>
</tr>
<tr>
<td>Mean aortic pressure (mmHg)</td>
<td>99</td>
<td>74</td>
<td>70</td>
</tr>
<tr>
<td>Pulmonary artery systolic pressure (mmHg)</td>
<td>122</td>
<td>83</td>
<td>52</td>
</tr>
<tr>
<td>Pulmonary artery diastolic pressure (mmHg)</td>
<td>57</td>
<td>38</td>
<td>24</td>
</tr>
<tr>
<td>Mean pulmonary artery pressure (mmHg)</td>
<td>82</td>
<td>55</td>
<td>37</td>
</tr>
<tr>
<td>Mean pulmonary artery wedge pressure (mmHg)</td>
<td>11</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Cardiac output</td>
<td>2.9</td>
<td>3.7</td>
<td>3.7</td>
</tr>
<tr>
<td>Cardiac index (l/min/m²)</td>
<td>1.83</td>
<td>2.34</td>
<td>2.34</td>
</tr>
<tr>
<td>Total pulmonary resistance (dyne S cm⁻⁵)</td>
<td>2,260</td>
<td>1,188</td>
<td>799</td>
</tr>
<tr>
<td>Pulmonary vascular resistance (dyne S cm⁻⁵)</td>
<td>1,957</td>
<td>972</td>
<td>583</td>
</tr>
<tr>
<td>Systemic vascular resistance (dyne S cm⁻⁵)</td>
<td>2,728</td>
<td>1,598</td>
<td>1,512</td>
</tr>
</tbody>
</table>

PaCO2 39.3 mmHg, and PaO2 101.4 mmHg while receiving oxygen, 1.5 l/min, by canula.

### Discussion

Epoprostenol (prostaglandin I₂) is a potent vasodilator and inhibitor of platelet aggregation normally produced by vascular endothelium (4–6). Long-term epoprostenol therapy reduces pulmonary vascular resistance and increases cardiac output with improvement of survival in PPH (7–10). Sueta
et al (11) studied patients with heart failure and reported that epoprostenol produced a significant decline in systemic and pulmonary vascular resistance and a substantial increase in cardiac index, but weaning of epoprostenol after 12 weeks of continuous infusion resulted in an increased mean pulmonary artery pressure and pulmonary vascular resistance. It is also reported that sudden withdrawal of epoprostenol can result in a severe rebound of pulmonary hypertension (12, 13).

On the other hand, symptomatic improvement sometimes remains after dose reduction of epoprostenol (14). Rich and McLaughlin (14) reported that careful dose reduction of epoprostenol by about 40% in PPH patients with high cardiac output did not cause rebound pulmonary hypertension. Okano et al (15) proposed the combination of intermittent, short-term intravenous epoprostenol and maintenance therapy with beraprost, an orally active prostacyclin analogue, for PPH. They reported that within a few months after initiation, epoprostenol could be tapered and successfully discontinued in three of five patients with PPH; symptomatic improvement was sustained despite the absence of hemodynamic benefits of epoprostenol. In the present case, discontinuation of epoprostenol after 24 days of infusion did not cause a rebound in pulmonary vascular resistance. The reason why pulmonary vascular resistance remained reduced even after discontinuation of epoprostenol is unknown. The patient has remained in good condition in New York Heart Association class III with low-flow supplemental oxygen and beraprost several months after discontinuation of epoprostenol.

Continuous infusion of epoprostenol is an established treatment in PPH. On the other hand, discontinuation of epoprostenol has been considered possible in a limited number of patients with PPH. The present case shows that short-term epoprostenol therapy can produce sustained symptomatic improvement even after discontinuation of therapy in a PPH patient. Further study is necessary to evaluate this mode of treatment in PPH.

References