Both aerosolized and intravenous infusion of iloprost caused a significant decrease in mean pulmonary artery pressure and pulmonary vascular resistance. Although intravenous infusion caused a large decrease in mean systemic arterial pressure, this was only slightly affected by aerosolized iloprost. Aerosolized iloprost caused a significant decrease in the pulmonary-to-systemic vascular resistance ratio; however, intravenous infusion did not cause a prominent decrease in this ratio. ©2003 by Excerpta Medica, Inc.

Comparison of Acute Hemodynamic Effects of Aerosolized and Intravenous Iloprost in Secondary Pulmonary Hypertension in Children With Congenital Heart Disease

Olgu Hallioglu, MD, Embiya Dilber, MD, and Alpay Celiker, MD

The present report compares the efficacy of the short-term administration of aerosolized and intravenous iloprost on pulmonary hemodynamics in children with pulmonary hypertension secondary to congenital heart disease.

Twelve children (median age 17 months; range 6 months to 16 years) with pulmonary hypertension secondary to congenital heart disease were included in the study. Patients’ demographic data are listed in Table 1. Pulmonary hypertension was defined as mean pulmonary artery pressure >30 mm Hg. The diagnosis of pulmonary hypertension was established by cardiac catheterization. Informed consent was obtained from parents before recruiting children to participate in the study.

The following protocol was used in all patients: (1) baseline hemodynamic measurements, (2) administration of 25 ng·kg⁻¹·min⁻¹ intravenous iloprost for 10 minutes, (3) after returning to baseline value, administration of 25 ng·kg⁻¹·min⁻¹ aerosolized iloprost for another 10 minutes. At the end of each application, hemodynamic results were assessed.

The children were premedicated with an intramuscular “cardiac cocktail” mixture of meperidine (2 mg/kg), promethazine (1 mg/kg), and chlorpromazine (1 mg/kg). Local anesthesia for femoral catheter insertion was achieved with lidocaine. During cardiac catheterization, patients were sedated with midazolam (dormicum 0.1 mg/kg intravenously [maximum dose 15 mg]).

Iloprost was obtained as an ethanol-buffered solution (Ilomedin; Schering AG, Berlin, Germany), which is approved in Turkey for general use. Intravenous iloprost with a dose of 25 ng·kg⁻¹·min⁻¹ for 10 minutes was prepared and diluted in 10 ml of isotonic saline solution. It was administered through a peripheral vein using a pump system. After baseline values were obtained, aerosolized iloprost was administered at the same dose of 25 ng·kg⁻¹·min⁻¹ diluted in 5 ml of isotonic saline solution and nebulized for another 10 minutes by way of the MicroDrop Master Jet (MPV, Truma, Germany) using a particle size of 3 µm to provide alveolar deposition of the substance.

Appropriate-sized introducer sheets were placed into both the femoral vein and artery. Intravascular pressures were measured concomitantly with fluid-filled transducers. Two transducers were positioned at...
## TABLE 1
Demographic and Hemodynamic Variables in Patients With Pulmonary Hypertension at Baseline and After Intravenous (IV) and Aerosolized Iloprost

<table>
<thead>
<tr>
<th>Patient Number</th>
<th>Diagnosis</th>
<th>Age (mo)</th>
<th>Weight (kg)</th>
<th>mPAP (mm Hg) Baseline</th>
<th>mSAP (mm Hg) Baseline</th>
<th>PVR (U·m⁻²) Baseline</th>
<th>Qp/Qs Baseline</th>
<th>IV</th>
<th>Inhaled</th>
<th>IV</th>
<th>Inhaled</th>
<th>IV</th>
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<td>1.5</td>
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<td>0.29</td>
<td>1.8</td>
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<td>18.44</td>
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Mean ± SD
- mPAP: Mean pulmonary artery pressure; mSAP: Mean systemic artery pressure; PVR: Pulmonary vascular resistance; Rp/Rs: Pulmonary-to-systemic blood flow ratio; VSD: Ventricular septal defect.

*p < 0.05 for baseline versus intravenous iloprost; †p < 0.05 for intravenous versus aerosolized iloprost. 

**Recent reports describing the acute hemodynamic effects of inhaled nitric oxide and aerosolized iloprost in children with pulmonary hypertension have demonstrated that short-term aerosolized iloprost can produce comparable effects lasting longer than intravenous administration.**

### Hemodynamic Parameters

- **mPAP:** Mean pulmonary artery pressure
- **mSAP:** Mean systemic artery pressure
- **PVR:** Pulmonary vascular resistance
- **Qp/Qs:** Pulmonary-to-systemic blood flow ratio

### Blood Pressure

- **Systolic:** 120–140 mm Hg
- **Diastolic:** 80–100 mm Hg

### Blood Flow

- **Pulse:** 60–100 beats per minute

### Oxygen Saturation

- **Arterial:** 90–95%
- **Venous:** ≤ 50%

### Heart Rate

- **Moderate:** 80–100 beats per minute

### Side Effects

- **Dizziness, headache, flushing, nausea, vomiting, and confusion.**

### Conclusion

Intravenous iloprost also caused a decrease in pulmonary artery pressure in all patients; however, a greater decrease occurred in systemic artery pressure than in pulmonary artery pressure. In contrast to inhaled iloprost, intravenous application did not cause a significant decrease in arterial pressure. Systemic arterial pressure only slightly decreased with aerosolized iloprost application. Intravenous iloprost produced significant changes from baseline during repeated measurements. Friedman's test was used to test for global changes. Significant differences were found between the end of each period of drug administration. Data were analyzed using the SPSS 8.0 software package. (SPSS Inc., Chicago, Illinois.)
equally effective in selectively lowering pulmonary vascular resistance. To our knowledge, this is one of the first studies comparing the acute hemodynamic effects of aerosolized iloprost with those of intravenous iloprost in secondary pulmonary hypertension in children with congenital heart disease.

In the present investigation, intravenous and aerosolized iloprost were effective in lowering pulmonary vascular resistance. Selectivity of aerosolized iloprost for pulmonary circulation was achieved, as indicated by a substantial decrease in pulmonary artery pressure and a small effect on systemic arterial pressure. In a previous study, it has also been shown that preferential distribution of aerosolized iloprost to the best-ventilated lung areas, which improved ventilation–perfusion matching, was seen by an increase in arterial oxygen saturation.1,10 In some studies, this effect was even found to be superior to that of inhaled nitric oxide, another selective pulmonary vasodilator in patients with pulmonary hypertension.3 The more potent acute effect of inhaled iloprost on pulmonary hemodynamics was reflected not only by a more pronounced decline of pulmonary artery pressure, but also by a prominent increase in pulmonary-to-systemic flow ratio. A limitation of this study was that we did not measure oxygen consumption during intravenous or inhaled iloprost administration. Because the intravenous application of iloprost showed a similar efficacy profile on both mean systemic artery and mean pulmonary artery pressures, it disrupted pulmonary hemodynamics. Clinically apparent hypotension was seen in 6 patients during intravenous administration.


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