gas. We assumed that endogenously produced droplets would be within the distribution of the exhaled gas. The spread of the exhaled gas may be greater than shown, as evaporation and reduction in density of the droplets at the margin of the plume may limit their effectiveness as markers. On the other hand, the visualized cloud does mark the minimum distribution of gas that originated in the lung.

In the mask without side vents, all exhaled gas traverses a manifold containing three valves and exits through a single port. Placing a bacterial/viral filter on this port may provide effective respiratory isolation during oxygen administration to spontaneously breathing patients.

The current recommendations for the management of SARS patients acknowledge the importance of the isolation of exhaled gas to prevent the release of infected droplets into the atmosphere. This can be accomplished with N95 or equivalent masks in spontaneously ventilating patients who do not require oxygen supplementation, and by the placement of bacterial/viral hydrophobic filters on the end of the endotracheal tube and/or the exhalation port of the self-inflating bag or breathing circuit in ventilated patients. However, when oxygen supplementation is required for spontaneously breathing patients, guidelines often condone open circuit administration to spontaneously breathing patients. In light of reports of SARS patients infecting other patients and health-care workers during the preintubation phase of their treatment, despite the use of protective equipment by health-care workers, we think that additional measures should be considered. The administration of oxygen using the delivery systems described in this article may further reduce the risk of the nosocomial transmission of respiratory infections such as SARS.

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REFERENCES

**Identical Twins With Primary Pulmonary Hypertension**

**Beraprost vs Epoprostenol**

Erika Berman Rosenzweig, MD; Kelly A. Schmitt, RN; Robert Garofano, PhD; and Robyn J. Barst, MD

**Background:** The course of 12-year-old, homozygotic twins with primary pulmonary hypertension (PPH) treated with different vasoactive agents, beraprost vs epoprostenol, is described.

**Methods:** Clinical, exercise, and hemodynamic assessments were made at baseline, and at 9 months and 24 months of treatment.

**Findings:** Twin A had a rapid improvement with epoprostenol. In contrast, twin B, initially treated with beraprost, had progressive worsening with subsequent improvement on epoprostenol.

**Interpretation:** Epoprostenol was efficacious for identical twins with PPH. A 9-month delay in initiating epoprostenol for twin B did not appear to have irreversible short-term detrimental effects.

(CHEST 2004; 125:1157–1160)

**Key words:** beraprost; epoprostenol; pulmonary hypertension

**Abbreviations:** PPH = primary pulmonary hypertension; VO₂ = oxygen consumption; WHO = World Health Organization

The course of 12-year-old, homozygotic twins with primary pulmonary hypertension (PPH) treated with different vasoactive agents is described (beraprost vs epoprostenol). Twin A was treated with continuous IV epoprostenol, is described. Twin B was initially treated with the oral prostacyclin analog beraprost, and was subsequently transitioned to epoprostenol.

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**Case Reports**

Twin A was a 12-year-old, otherwise healthy child who presented to her pediatrician with recurrent syncopal episodes with exertion. She denied other symptoms. Her physical examination was significant for a grade 1/6 systolic murmur at the left lower sternal border, grade 1/6 diastolic murmur at the left upper sternal border, and a prominent P2 component. A workup was performed, and World Health Organization (WHO) functional class III PPH was diagnosed. Twin B was a 12-year-old, otherwise healthy child who received a diagnosis of PPH at the same time her sister presented, when she complained of jaw and right arm pain. Her physical examination was significant for a grade 1/6 systolic murmur at the left lower sternal border, grade 1/6 diastolic murmur at the left upper sternal border, and a prominent P2 component. A cardiopulmonary workup was performed, and WHO functional class II PPH was diagnosed.

Cardiopulmonary catheterization demonstrated severe pulmonary arterial hypertension with no significant acute response to inhaled nitric oxide for either patient (Table 1). Due to the potentially catastrophic nature of syncopal episodes as well as being more symptomatic than her sister, and the 50% chance of being treated with a placebo in the placebo-control beraprost trial, twin A was treated with IV epoprostenol (initiated at 4 ng/kg/min and titrated upward as needed). After discussing overall risk/benefit considerations, twin B was started on the oral prostacyclin analog beraprost.

**Table 1—Hemodynamics at Baseline (Pretreatment), 9 Months, and 24 Months**

<table>
<thead>
<tr>
<th>Hemodynamics</th>
<th>Twin A, Epoprostenol</th>
<th>Twin B, Beraprost</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>9 Months</td>
</tr>
<tr>
<td>PAP, mm Hg†</td>
<td>71 (107/50)</td>
<td>51 (79/30)</td>
</tr>
<tr>
<td>SAP, mm Hg†</td>
<td>75 (99/61)</td>
<td>74 (104/56)</td>
</tr>
<tr>
<td>RAPm, mm Hg</td>
<td>13</td>
<td>3</td>
</tr>
<tr>
<td>MVsat, %</td>
<td>63</td>
<td>70</td>
</tr>
<tr>
<td>CI, L/min/m²</td>
<td>1.6</td>
<td>2.0</td>
</tr>
<tr>
<td>SVRi, U × m²</td>
<td>43</td>
<td>35</td>
</tr>
<tr>
<td>PCWPm, mm Hg</td>
<td>8</td>
<td>7</td>
</tr>
</tbody>
</table>

*PAP = pulmonary arterial pressure; SAP = systemic arterial pressure; RAPm = mean right atrial pressure; MVsat = mixed venous saturation; CI = cardiac index; PVRi = pulmonary vascular resistance index; SVRi = systemic vascular resistance index; PCWPm = mean pulmonary capillary wedge pressure.
†Data presented as mean (systolic/diastolic).

**Cardiopulmonary Exercise Testing - Exercise Tolerance**

![Figure 1. Peak VO2 at baseline (BL), and at 9 months, 12 months, 18 months, and 24 months for twin A vs twin B. Note that twin B transitioned to epoprostenol following the 9-month visit.](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/20385/)
Considered the epoprostenol. Historically, epoprostenol has been considered the gold standard for patients with PPH who are nonresponsive to calcium-channel blockers. However, there are potentially catastrophic risks associated with the use of epoprostenol due to the IV delivery system. Despite the risks, epoprostenol has significant efficacy, improved quality of life, hemodynamics, exercise capacity, and survival. In the past several years, efforts have focused on developing alternative delivery systems for prostacyclin. Oral beraprost has been used empirically in Japan, and was shown to increase exercise capacity in a 12-week, multicenter, double-blind, randomized, placebo-controlled European trial. Beraprost was also shown to transiently improve exercise capacity at 3 months and 6 months, but not at 9 months or 12 months, in a 12-month, multicenter, double-blind, randomized, placebo-controlled randomized US trial.

Our report illustrates the favorable response of twin A to epoprostenol in comparison to the worsening course of twin B with beraprost. It remains unclear to what degree her clinical worsening was related to the relatively short half-life of beraprost (1.5 h), preventing a steady state with four-times-daily dosing; and/or its side effects, which precluded increasing to a more efficacious dose. Regardless, once twin B discontinued beraprost and started epoprostenol, she significantly improved, documented by serial exercise and hemodynamic data. While epoprostenol dosing increases are often limited by patient side effects, it appears that for this child, at the beraprost and epoprostenol doses that were tolerated, epoprostenol had a better risk/benefit profile.

This case report also raises questions about the timing of institution of effective therapy for PPH. Although twin B remains slightly more symptomatic than her sister with epoprostenol, she has only been receiving epoprostenol for 15 months; her sister has been treated for 24 months. Twin B is clearly responsive to epoprostenol despite the delay in instituting epoprostenol for 9 months. These data are encouraging since intuitively we hypothesize that earlier diagnosis and, thus, earlier treatment may improve outcome. This report raises the possibility that there is a "window" for institution of treatment that ensures an optimal or near-optimal therapeutic response. This may have important implications for treatment planning, particularly with various agents now available: one may elect to start a patient on an oral agent (eg, endothelin receptor antagonist, phosphodiesterase inhibitor, or prostacyclin analog) before considering epoprostenol. Further investigation is warranted as this "therapeutic window" likely differs among patients.

Conclusions

Epoprostenol was efficacious for two identical twins with PPH. A 9-month delay in initiating epoprostenol for twin B did not appear to have irreversible short-term detrimental effects; however, long-term follow-up is needed to determine whether there are long-term benefits with early initiation of epoprostenol.

References

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