BRIEF COMMUNICATIONS

AEROSOLIZED PROSTACYCLIN (EPOPROSTENOL) AS AN ALTERNATIVE TO INHALED NITRIC OXIDE FOR PATIENTS WITH REPERFUSION INJURY AFTER LUNG TRANSPLANTATION

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Treatment options for patients with severe reperfusion injury after lung transplantation often include the use of inhaled nitric oxide. However, the recent escalation in cost has made its use somewhat prohibitive. Here we describe the technique of using inhaled prostacyclin (epoprostenol), as opposed to using inhaled nitric oxide, for the treatment of lung transplant reperfusion injury. We believe this is the first reported case of its use in this setting.

Clinical summary. A 51-year-old man underwent single lung transplantation for chronic obstructive pulmonary disease. Severe reperfusion injury subsequently developed, with an oxygenation index of greater than 30.¹ The chest radiograph showed almost complete white-out of the transplanted lung. Mean pulmonary artery pressures preoperatively were 24 mm Hg. Mean pulmonary artery pressures after lung transplantation were 35 to 40 mm Hg. This patient was subsequently treated by arteriovenous extracorporeal membrane oxygenation (ECMO). After the start of ECMO, mean pulmonary artery pressures remained at 35 to 40 mm Hg. Given this, we were concerned that the patient had ongoing reperfusion injury. We and others have thought that pulmonary vasodilators, such as inhaled nitric oxide, help to decrease reperfusion injury by decreasing pulmonary vascular resistance and increasing pulmonary artery blood flow.² However, given the substantial cost of inhaled nitric oxide, we instead chose to administer inhaled, aerosolized prostacyclin at a rate of 50 ng · kg⁻¹ · min⁻¹ using an in-line circuit and MiniHeart nebulizer chamber (Vortran Medical Technology, Inc, Sacramento, Calif) (Table I). After institution of aerosolized prostacyclin, mean pulmonary artery pressures dropped to 25 to 30 mm Hg. After 48 hours the patient was weaned from ECMO and continued receiving inhaled prostacyclin for an additional 24 hours. This patient eventually recovered and was discharged to his home on hospital day 11.

Comment. Nitric oxide has often been used as an adjunctive measure for the treatment of reperfusion injury with some success.² However, the recent cost increase in inhaled nitric

Table I. Aerosolized prostacyclin protocol for lung transplant recipients

- 1 Lung transplant patients with elevated pulmonary artery pressures (mean pulmonary artery pressure > 20 mm Hg or pulmonary vascular resistance > 200 dynes · s · cm⁻⁵) and a low cardiac index (cardiac index < 2.5 L · min⁻¹ · m⁻²) owing to right heart failure
- 2 Patients with right heart failure owing to left heart failure are excluded
- 3 Initial dose of inhaled epoprostenol is 50 ng · kg⁻¹ · min⁻¹
- 4 If the initial dose causes a decrease in systemic blood pressure by more than 10%, the rate is decreased to 25 ng · kg⁻¹ · min⁻¹
- 5 The initial dose is cut in half every 15 minutes to find the lowest effective dose

oxide has made its use somewhat prohibitive. In this report, we demonstrate the technique of using inhaled prostacyclin in patients with reperfusion injury. We have also identified some potential advantages of inhaled prostacyclin over inhaled nitric oxide.

In this patient, inhaled prostacyclin was effective at decreasing the elevated pulmonary artery pressures associated with reperfusion injury. We and others believe decreasing pulmonary artery pressure lessens water accumulation and injury to the transplanted lung.³ To our knowledge, no other authors have reported on the clinical use of inhaled prostacyclin for the treatment of lung transplant reperfusion injury. Some clinical studies, however, have investigated the effect of inhaled prostacyclin on acute respiratory distress syndrome.^{4,5} Van Heerden and associates⁴ demonstrated effective use of inhaled prostacyclin in 9 patients with acute respiratory distress syndrome. Those authors demonstrated a significant dose-dependent improvement in arterial oxygenation/percent inhaled oxygen ratio after administration of inhaled prostacyclin. No significant complications resulted from the use of the drug.

Some animal studies have demonstrated the beneficial effects of *intravenous* prostacyclin in reducing lung transplant reperfusion injury.^{6,7} Matsuzaki and colleagues⁶ demonstrated reduced reperfusion injury in a rabbit model after intravenous prostacyclin. Okada and coworkers⁷ similarly demonstrated reduced reperfusion injury in a rat model after the administration of intravenous prostacyclin. Although these investigations show improvement in lung reperfusion injury after the administration of intravenous prostacyclin, to our knowledge only one animal study has shown an improvement in reperfusion injury after the administration of inhaled prostacyclin.³

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One advantage of inhaled prostacyclin is that it avoids the possible buildup of oxygen radicals associated with inhaled nitric oxide. Some authors have questioned whether or not a toxic buildup of oxygen radicals occurs with the use of nitric oxide.^{8,9} Murakami and coworkers⁸ demonstrated improvement in reperfusion injury after administration of nitric oxide at low doses, although higher doses seemed to worsen reperfusion injury. Eppinger and coworkers⁹ found similar results.

Another advantage of inhaled prostacyclin is that it is also less expensive than inhaled nitric oxide. Patient charges at our institution for inhaled nitric oxide are \$5500 a day regardless of amount used. In comparison, inhaled prostacyclin costs \$960 a day at a dosage of $50 \text{ ng} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$, which is the recommended maximal clinical dosage.

In summary, inhaled prostacyclin appeared to be as effective as inhaled nitric oxide, may have the advantage of avoiding the potential buildup of oxygen radicals, and is cheaper than nitric oxide. Thus, inhaled prostacyclin should be considered in patients with severe reperfusion injury after lung transplantation.

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