

# Anesthetizing the Child with Pulmonary Arterial Hypertension

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## Conflicts of Interest

I have no relevant financial or professional conflicts of interest to report.

## Objectives

At the conclusion of this presentation the participant should be able to

1. Appreciate the increased perioperative risk associated with pulmonary hypertension..
2. Know potential perioperative triggers and the mechanism of cardiac failure associated with a pulmonary hypertensive crisis.
3. Understand the principles of perioperative care in children with pulmonary hypertension.
4. Be aware of new developments in acute pulmonary vasodilator therapy.

## Introduction

Pulmonary arterial hypertension (PAH) is defined as the presence of a mean pulmonary artery pressure that exceeds 25 mmHg at rest or 30mmHg during exercise. PAH can be idiopathic (primary) or associated with a variety of underlying causes including congenital heart disease, chronic lung disease, chronic airway obstruction, and chronic liver disease. PAH is associated with significant perioperative risk for major complications. It is important that anesthesiologists be aware of this increased risk, understand the pathophysiology of PAH, form an appropriate anesthetic management plan, and be prepared to treat a pulmonary hypertensive crisis.

## Cardiovascular Risks

Several mechanisms can be associated with hemodynamic deterioration in patients with PAH. Hypercarbia, hypoxia, acidosis, and noxious stimuli such as pain and airway instrumentation can trigger a rapid increase in PVR that can lead to a pulmonary hypertensive crisis and/or right heart failure. A pulmonary hypertensive crisis is characterized by a rapid increase in PVR to the point where pulmonary artery pressure (PAP) exceeds systemic blood pressure. The resulting right heart failure leads to a decrease in pulmonary blood flow, decreased cardiac output, hypoxia, coronary hypoperfusion, and biventricular failure. Right ventricular dilation is associated with leftward displacement of the interventricular septum, leading to inadequate filling of the left ventricle, decreased stroke volume, and decreased cardiac output. Systemic hypotension or a decrease in systemic vascular resistance (SVR) can cause a decrease in coronary artery blood flow, leading to biventricular ischemia. Risk of perioperative complications is greater in patients with supra-systemic PAH and in those having major surgery. Risk may be less in patients who are treated with pulmonary vasodilators preoperatively.

## Treatment of Pulmonary Hypertensive Crisis

The goals of treatment are to vasodilate the pulmonary vasculature, support cardiac output, and remove stimuli associated with increases in PVR.

1. *Administer 100% oxygen.* Increasing PO<sub>2</sub> can decrease PVR.
2. *Hyperventilate to induce a respiratory alkalosis.* PAP was directly related to PCO<sub>2</sub> in mechanically ventilated children with congenital heart disease.
3. *Correct metabolic acidosis.* PVR is directly related to H<sup>+</sup> concentration.

4. *Administer pulmonary vasodilators.* Inhaled nitric oxide (iNO) is generally the first drug of choice; intravenous or inhaled prostacyclin analogs are effective.
5. *Support cardiac output.* Adequate preload is important. Inotropic support is often necessary. A variety of inotropic drugs can be used. Dobutamine reduces PVR, but often dopamine is preferred in order to maintain SVR and enhance coronary perfusion.
6. *Attenuate noxious stimuli* (provide analgesia). Noxious stimuli, such as pain and tracheal suctioning, can increase PVR. These responses can be attenuated by pretreatment with fentanyl.

### **Anesthetic Management**

The goals of anesthetic management are to provide adequate anesthesia and analgesia for the surgical procedure, minimize stimuli for pulmonary vasoconstriction, minimize systemic cardiovascular depression, and maintain the ability to treat increases in PVR if they occur. Depending on the procedure, these goals can be successfully met by sedation/analgesia, regional analgesia, or general anesthesia. Although tracheal instrumentation can trigger an increase in PVR, airway management method (natural airway, laryngeal mask airway, or endotracheal tube) should be appropriate for the surgical procedure. Since the anesthesiologist must maintain the ability to immediately assist or control ventilation, the use of endotracheal tubes and laryngeal mask airways is often preferred.

No single anesthetic agent is ideal for patients with PAH. Many anesthetics exhibit mixed hemodynamic effects, such as pulmonary vasodilatation along with depression of myocardial contractility, and may be unacceptable when used in full anesthetic dosage. The pulmonary vascular effects of most anesthetic drugs have been incompletely studied, particularly in the presence of PAH. We usually employ a balanced anesthetic technique, in which subanesthetic doses of several drugs are combined to provide general anesthesia. Typically, we use oral or intravenous midazolam for premedication. Induction is cautiously achieved with midazolam, fentanyl, a small dose of propofol, and/or a low concentration of sevoflurane. Anesthesia is maintained with intermittent fentanyl and isoflurane or sevoflurane. Rocuronium or pancuronium are used for neuromuscular blockade as indicated. Perioperative use of pulmonary vasodilators is recommended in patients with significant PAH.

### **Pulmonary Vasodilators**

*Inhaled nitric oxide* (iNO) provides selective pulmonary vasodilation and is often the first drug of choice for intraoperative use because of its effectiveness, rapid onset, and ease of administration. iNO bypasses the damaged pulmonary vascular endothelium present in pulmonary hypertensive disorders and diffuses into the vascular smooth muscle cell, where it activates soluble guanylate cyclase. This increases cGMP concentrations resulting in vasodilation. In children with systemic or suprasystemic PAH, we administer iNO through the breathing circuit intraoperatively beginning with anesthetic induction. Postoperatively, it is continued via mask or nasal cannulae until the patient is stable and weaned over time. Rebound pulmonary hypertension following weaning of iNO can occur, especially after a prolonged or severe pulmonary hypertensive episode. iNO is expensive, so other pulmonary vasodilators suitable for acute therapy are being investigated as alternatives.

*Prostacyclin* analogs cause vasodilation by increasing cAMP concentration through stimulation of adenylate cyclase and have proven to be highly effective in the treatment of PAH. They are characterized by rapid onset of action and very short half-lives. Epoprostenol, the most studied, is administered by continuous intravenous infusion; chronic therapy has improved

the five-year survival of children with idiopathic PAH. Many children with idiopathic PAH who are on epoprostenol therapy require anesthesia for central venous line placement or replacement; it is important that the epoprostenol infusion remain uninterrupted because of its extremely short half-life. The inhaled prostacyclin analog, iloprost, has been shown to be as effective as iNO in the short term reduction of PVR in children with congenital heart disease. It is also effective for long term therapy, but is associated with bronchoconstriction in some patients. Iloprost is administered as an aerosol by nebulization.

*Phosphodiesterase (PDE) inhibitors* block the hydrolysis of cGMP, thus increasing the concentration of cGMP in the vascular smooth muscle cell. The PDE-5 inhibitors, sildenafil and dipyridamole, are highly effective pulmonary vasodilators with rapid onset of action and the ability to attenuate rebound hypertension following withdrawal of iNO. Sildenafil is currently only approved for enteral use (if needed intraoperatively, it can be administered via a nasogastric tube); however, intravenous sildenafil is effective, and this use is expected to be approved soon. Milrinone, a PDE-3 inhibitor, is a less specific blocker of cGMP hydrolysis, but is often used perioperatively because it decreases PVR while augmenting myocardial contractility. Milrinone has been successfully administered by inhalation.

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