

Chapter

40

Idiopathic Pulmonary Hypertension

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Case Scenario

A 10-year-old female with newly diagnosed idiopathic pulmonary hypertension is scheduled for placement of a peripherally inserted central catheter in Interventional Radiology. Two weeks prior she presented to the emergency department after a syncopal episode, and her parents reported a history of progressive dyspnea on exertion with even minimal activity. Her SpO₂ on room air was 89%.

Transthoracic echocardiography at that time revealed:

- *Right ventricular hypertrophy with suprasystemic right ventricular pressures*
- *Mild right ventricular dysfunction*

Cardiac catheterization the following day confirmed the diagnosis of pulmonary hypertension, demonstrating pulmonary artery pressures 20 mm Hg greater than systemic, a pulmonary vascular resistance of 15 indexed Wood units and no response to nitric oxide administration. She was started on oral bosentan and sildenafil, intravenous treprostinil, and oxygen via nasal cannula. She remained in the intensive care unit as her medications were titrated to effective doses. She now requires long-term central access for continuous intravenous treprostinil therapy prior to discharge home. She has extreme anxiety and is very fearful about the proposed procedure.

Key Objectives

- Discuss clinical signs and symptoms leading to a diagnosis of idiopathic pulmonary hypertension.
- Describe the classes of medications available for treatment of these patients.
- Discuss anesthetic risk for these patients and discussion of risk with the family.
- Describe perioperative care and airway management strategies for this patient.

Pathophysiology

What is the definition of pulmonary hypertension? How does it differ from pulmonary arterial hypertension?

According to the Paediatric Task Force of the 6th World Symposium on Pulmonary Hypertension in 2018, pulmonary hypertension is defined in adults and children as a mean pulmonary artery pressure (mPAP) >20 mm Hg at rest. Normal mPAP at rest is 15 mm Hg.

Pulmonary arterial hypertension (PAH) is a subset of PH and is defined as PH due to pulmonary vascular disease, with elevated pulmonary vascular resistance (PVR) >3 indexed Wood units (iWU or WU/m²) alongside a normal pulmonary capillary wedge pressure (PCWP) <15 mm Hg.

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Pulmonary arterial hypertension is a subset of PH due to pulmonary vascular disease and is defined by a mean PAP >20 mm Hg at rest and PVR >3 iWU with normal PCWP.

What is the pathophysiology of PAH?

Pulmonary arterial hypertension is a structural pulmonary vascular disease in which smooth muscle cell proliferation and endothelial cell dysfunction lead to a progressive narrowing of the pulmonary vasculature. Additionally, patients with PAH have an imbalance of vasoactive mediators. The production of normally abundant vasodilators, such as nitric oxide and prostacyclin, is decreased, while pulmonary vasoconstrictors, such as endothelin-1 and serotonin, are increased. Both processes combine to cause intravascular thrombosis, vascular remodeling, and eventual destruction of the pulmonary arterioles leading to pulmonary precapillary restriction to blood flow and an increase in the PVR. Initially, vasoconstriction is the major contributor and the changes are reversible. However, as the remodeling continues, the vessels reach an

irreversible point where they are no longer able to respond to physiologic signals to vasodilate. This results in right ventricular (RV) pressure overload leading to RV failure, and ultimately if untreated, death.

How is PH classified in children?

According to the 5th World Symposium on Pulmonary Hypertension, PH can be grouped into one of five categories based on etiology:

1. *Pulmonary arterial hypertension (PAH)*

- 1.1. Idiopathic
- 1.2. Heritable
- 1.3. Drug and toxin induced
- 1.4. Congenital heart disease associated

1'. Pulmonary veno-occlusive disease

1''. Persistent pulmonary hypertension of the newborn (PPHN) (see Chapter 46)

2. *Pulmonary hypertension due to left heart disease*

3. *Pulmonary hypertension due to lung diseases and/or hypoxia*

4. *Chronic thromboembolic pulmonary hypertension*

5. *Pulmonary hypertension with multifactorial mechanisms*

What is the World Health Organization Functional Classification for PH and why is it important?

The World Health Organization (WHO) Functional Classification describes the level of physical disability (dyspnea, fatigue, chest pain) caused by a patient's PH. It is predictive of mortality and is used when choosing a treatment plan. Levels III (symptoms at minimal activity) and IV (symptoms at rest and symptoms of right heart failure) are considered to be significant negative prognostic factors. (See Table 40.1.)

Clinical Pearl

World Health Organization Functional Class III (symptoms at minimal activity) and level IV (symptoms at rest and symptoms of right heart failure) are significant negative prognostic factors in PH patients.

What is idiopathic pulmonary arterial hypertension?

Idiopathic pulmonary arterial hypertension (IPAH) is the most common cause of pediatric PAH and has no known

Table 40.1 WHO Functional Classification for Pulmonary Hypertension

Functional Class	Symptoms
I	No limitation of physical activity
II	Comfortable at rest. Ordinary activity causes dyspnea, fatigue, chest pain, or syncope
III	Comfortable at rest. Less than ordinary activity causes dyspnea, fatigue, chest pain, or syncope
IV	Dyspnea, fatigue, or chest pain at rest that is increased with any activity. Symptoms of right heart failure

underlying cause, and thus is a diagnosis of exclusion. Presenting symptoms of IPAH are vague and nonspecific, which often leads to a delay between onset and diagnosis. Infants and younger children may present with feeding difficulties, failure to thrive, tachypnea, and irritability due to low cardiac output. The most common complaint in older children is a gradual reduction in exercise capacity, associated with fatigue and dyspnea. Other less common presenting signs include chest pain, cyanosis, cough, or syncope. Syncope as a presenting symptom of IPAH is more common in pediatric patients than in the adult population.

How is PAH diagnosed?

Echocardiography is often used as a noninvasive screening tool for the diagnosis of PAH. It can provide direct and indirect evidence of elevated PAP, evaluate RV function, and may offer information regarding etiology to aid in prognosis.

Important echocardiographic indices include the following:

- The **velocity of a tricuspid regurgitant jet** (TR) can be used to give a quantitative estimate of RV pressure, with values greater than 2.8 m/second suggestive of RV hypertension. However, a trivial or inconsistent TR jet may lead to underestimation of disease severity.
- **Flattening of the interventricular septum** is indicative of systemic RV pressures, whereas bowing of the septum to the left indicates suprasystemic RV pressures.
- **Bidirectional or reverse flow of intra- or extracardiac shunts** also indicates elevated RV pressure.

Cardiac catheterization is the gold standard for the diagnosis of PAH and is necessary for the assessment of disease severity and treatment stratification. A right heart catheterization can be performed to evaluate intra- or extracardiac shunts, to measure mPAP, PVR, and PCWP for

diagnosis, and to perform acute vasoreactivity testing (AVT) to guide therapy. Cardiac catheterization is also recommended prior to the initiation of medical therapy, to evaluate the effectiveness of medical therapy, and for assessment during times of clinical deterioration.

What is acute vasoreactivity testing?

During cardiac catheterization, a pulmonary vasodilator, usually inhaled nitric oxide (iNO), is administered to determine whether it will acutely lower PVR. A positive test is defined as a >20% fall in mPAP with either no change or a decrease in the ratio of pulmonary vascular resistance to systemic vascular resistance (PVR/SVR) without a decrease in cardiac output (CO). A positive AVT result indicates a better prognosis because it reflects preserved vascular reactivity, suggesting a reversible component to the elevated PVR. It also identifies those patients who will benefit from targeted PAH therapy.

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A positive AVT test is defined as a >20% fall in mPAP and either no change or a decrease in PVR/SVR without a decrease in cardiac output. A positive AVT result indicates a better prognosis because it reflects preserved vascular reactivity, suggesting a reversible component to the elevated PVR.

What are the goals of medical therapy for PAH?

The advent of targeted therapies for PAH has significantly improved the outcomes of children living with this diagnosis, yet despite these advances, PAH remains an incurable disease. The goals of therapy, therefore, are to optimize quality of life and enhance survival by halting disease progression. Medications are used to target reversible changes by promoting pulmonary arterial vasodilation and improving RV function. Therapeutic decisions are based on the results of AVT testing as well as risk stratification.

What are the initial treatment options after diagnosis of PAH?

The American Heart Association and American Thoracic Society have established an algorithm for the treatment of PAH. Supportive therapies are first initiated at diagnosis to help minimize morbidity and control the symptoms related to PAH.

- **Oxygen supplementation** is often utilized for saturations <92% to mitigate hypoxic-induced pulmonary vasoconstriction.
- **Medical therapies** are directed toward the treatment of RV failure.
 - *Diuretics* help offload the RV but should be used with caution, as PAH patients can be dependent on preload to maintain CO.
 - *Digoxin* may also be used to improve RV function.
- **Anticoagulation** is sometimes employed due to the increased risk of thrombosis that contributes to the rise in PVR.

Once supportive medications are started, AVT is performed and used to guide further therapy.
- **Positive AVT:** Patients who are >1 year of age without RV failure are started on oral calcium channel blockers such as nifedipine, diltiazem, or amlodipine.
- **Negative AVT or failure to respond to CCB:** Patients are started on targeted therapy.

What are targeted therapies for PAH?

Current treatment strategies are aimed at improving the balance between vasodilation and vasoconstriction, preventing thrombosis from forming in narrow vessels, and attenuating vascular remodeling using antiproliferative drugs.

Three primary pathways are targeted to treat PAH: the endothelin pathway, the nitric oxide pathway, and the prostacyclin pathway.

- **Endothelin receptor antagonists (ERA)** block the action of endothelin, a pulmonary vasoconstrictor that is overexpressed in PAH. Medications in this class include bosentan, ambrisentan, and macitentan, all of which are administered orally. They can cause hepatotoxicity; therefore, liver function tests should be monitored closely.
- **Phosphodiesterase type 5 inhibitors (PDE5i)** reduce the breakdown of cGMP resulting in pulmonary vasodilation. They may also possess some antiproliferative properties. Phosphodiesterase inhibitors include sildenafil and tadalafil, which are both oral medications. Side effects include headache, flushing, and nasal congestion, necessitating slow titration.
- **Prostacyclin analogs (prostanoids)** provide an exogenous source of this potent pulmonary vasodilator, which is underexpressed in patients with PAH. This class of medications has also been shown to have antiplatelet, antithrombotic, antiproliferative, and anti-inflammatory properties. There are oral (treprostinil, beraprost), inhaled (treprostinil, iloprost), intravenous (IV) (epoprostenol, treprostinil), and subcutaneous (treprostinil) formulations available. **It is important to**

recognize the short half-life of IV forms. Intravenous epoprostenol has a half-life of 2–5 minutes and must be continuously infused 24 hours a day via a central venous line (CVL). Discontinuation puts the patient at risk for an acute PH crisis. Intravenous treprostinil (which also requires central administration) has a longer half-life of 2–4 hours, allowing more time if medication is discontinued until an acute PH crisis ensues. Similar to PDE5i, prostanoids may cause headaches, flushing, and nasal congestion, as well as abdominal pain.

How is appropriate targeted therapy chosen?

Patients who do not have a positive response to AVT or who fail CCB therapy are placed on targeted therapy after risk stratification.

- **WHO functional class I and II** (lower risk patients) are started on oral therapy with ERA or PDE5i with or without the addition of an inhaled prostacyclin.
- **WHO functional class III and IV** (higher risk patients) or those with deterioration on oral therapy are started on aggressive combination therapy (commonly referred to as **triple therapy**) using a medication from each of the receptor pathways.

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“Triple therapy” utilizes one medication from each of the three pulmonary vasodilator pathways: an endothelin receptor antagonist, a phosphodiesterase inhibitor, and a prostanoid. Both triple therapy and the need for intravenous PH therapy are indicative of severe PH.

What are the procedural options for the treatment of PAH?

Procedural interventions are reserved for patients who are still decompensating despite maximal medical therapy.

- An **atrial septostomy** can be created in the catheterization lab to augment left ventricular (LV) preload by serving as a “pop-off” valve, allowing shunting of blood from R-to-L during times of high right-sided pressures.
 - The ability to shunt R-to-L can worsen hypoxia. It is not performed on patients with oxygen saturations <90% or high right atrial pressure (>20 mm Hg), as excessive R-to-L shunting can then occur.
 - Without such a shunt, during times of increased PVR, less blood is able to get through the pulmonary system to the LV and CO will decrease.

- A **Potts shunt**, a surgically created anastomosis between the left pulmonary artery and the descending aorta, is an alternative to atrial septostomy.
 - Physiologically it achieves a similar result to an atrial septostomy by unloading the RV and providing systemic blood flow.
 - Because shunted blood enters the aorta beyond the coronary and cerebral circulations, these vessels will receive oxygenated blood from the LV, possibly offering an advantage over septostomy.

These treatments are both palliative efforts. The only definitive treatment for PAH is lung transplantation, or if the RV is severely damaged, a combined heart–lung transplant. Both operations carry significant morbidity and mortality.

Anesthetic Implications

What is known about anesthetic risk in patients with PH?

Assessing anesthetic risk in children with PH is difficult due to the heterogeneity among studies, as well as heterogeneity among the children themselves. Regardless, data show children with PH have a 20-fold higher incidence of perioperative cardiac arrest compared to the general pediatric population (1%–5% vs. 0.014%, respectively). Approximately 20% will have a change in oxygen saturation, carbon dioxide (CO₂), blood pressure, or mPAP that is unrelated to the type of procedure, anesthetic, or their specific type of PH. Pulmonary hypertensive crises have been reported in 2% and the risk of perioperative death has also been reported to be as high as 1.5%.

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Children with PH have a 20-fold higher incidence of perioperative cardiac arrest compared to the general pediatric population.

How is risk stratified in PH patients?

Not all patients with PH present with the same risk; therefore, preoperative risk stratification is imperative in preparing an appropriate anesthetic plan and determining the need for cardiovascular drug preparation, advanced life support availability (including extracorporeal membrane oxygenation [ECMO] backup), and postsurgical recovery location. Risk stratification requires evaluation of available diagnostic data, patient medication and functional status, as well as contributing anesthetic and surgical factors.

Cardiac catheterization: Factors placing patients in a high-risk category include systemic or suprasystemic RV and PA

pressures (ratio of mean PA pressure to mean systemic pressure >70%), elevated RA pressure (>10–15 mm Hg), and decreased cardiac index (<2.5 L/minute/m²). A PVR greater than 15 iWU and PVR/SVR ratio >1 are also considered severe.

Echocardiography: Signs of severe PH include evidence of significant RV enlargement, dysfunction, or failure; septal flattening or bowing into the LV; systemic or suprasystemic RV pressures; and bidirectional shunting or reversal of shunting. The presence of either a surgically created pulmonary to systemic (Potts) shunt or a percutaneously created atrial septal defect for therapeutic management of elevated right-sided pressures also reflects severe PH.

Medications: The patient's current medical therapies also provide a clue to disease severity. Escalation of care, the use of multidrug therapy, IV or subcutaneous medication administration, and home oxygen use are all suggestive of significant disease.

Signs and symptoms: Other indicators of PH severity include WHO class III/IV, syncope, chest pain, fatigue, dyspnea, cyanosis, and failure to thrive.

In addition to patient factors, the type of operation and timing of surgery also have an impact on anesthetic risk, with emergency surgery, major thoracic or abdominal surgeries, and anesthetic duration >3 hours considered higher risk.

What is involved in preoperative planning?

Due to the complexity and higher perioperative risk in patients with PH, a preoperative multidisciplinary team discussion is advised to ensure a careful plan is in place to mitigate this risk. Planning should include the anesthesiologist (who preferably has experience with PH patients), cardiologist, and proceduralist, all of whom can offer unique insights into care of the patient. Specific issues to address include the urgency and timing of the procedure, patient optimization, intraoperative concerns, and postoperative disposition. Patients with PH should be cared for in a setting capable of providing advanced life support and intensive care in the event of acute decompensation or cardiac arrest.

What are the preoperative considerations for a patient with IPAH?

Optimization: Care must be taken to ensure the patient has been medically optimized and has not been experiencing acute PH exacerbations. However, in this case, placement of the peripherally inserted central catheter (PICC) line will provide access for ongoing medical therapy and will

likely be necessary despite exacerbations. The most recent imaging data, cardiac catheterization and medication regimen must be reviewed. It is imperative that the patient be under the active care of a cardiologist.

Medication: Maintain the home regimen of PH medications, as even small interruptions can result in increases in PVR. Oral medications can be taken with a small sip of water on the day of surgery. Continuously delivered PH medications via inhaled, subcutaneous, and/or IV routes must remain uninterrupted. Any indwelling catheter delivering these medications should be considered a dedicated line and never used by the anesthesiologist. The use and management of anticoagulant, antihypertensive, and diuretic medications should also be discussed with the cardiologist. The surgical team should be aware of planned strategies for management of anticoagulation therapies.

Nil per os (NPO) status: Dehydration leads to decreased preload and is poorly tolerated. Consideration should be given to scheduling the patient as the first case of the day to minimize NPO time and intake of clear fluids up to 2 hours prior to the procedure should be encouraged. Patients at higher risk may benefit from overnight preoperative admission for IV hydration or should have IV fluids started in the holding area while waiting for their procedure.

Illness: Patients with PH who present with an acute respiratory infection or reactive airway exacerbation are at increased risk for a PH crisis. Gastrointestinal illness may lead to dehydration and decreased preload. Elective cases should be cancelled under these circumstances.

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The home medication regimen should be maintained throughout the perioperative period, as even small interruptions can result in increases in PVR. Continuously delivered PH medications via inhaled, subcutaneous, and/or IV routes should remain uninterrupted. Intravenous medications should run via a dedicated line that is not used by the anesthesiologist.

What are the goals in the anesthetic management of patients with IPAH?

The primary anesthetic management goal is to avoid increases in PVR while maintaining SVR, preload, and RV contractility. Maintenance of hemodynamic stability is crucial in this population, as even small hemodynamic deviations can overwhelm compensatory mechanisms and lead to a PH crisis.

What is a PH crisis and what factors can precipitate it?

A PH crisis is a sudden and potentially lethal increase in PVR that causes an unsustainable rise in the afterload of the RV leading to RV failure. This results in decreased LV preload with a fall in both CO and coronary perfusion, which, in turn, results in biventricular failure. If the PH crisis is not rapidly and aggressively treated, this cycle can lead to cardiac arrest. (See Figure 40.1.)

Acute increases in PVR can be precipitated by hypoxia, hypercarbia, acidosis, and hypothermia. Normothermia should be maintained during the perioperative period. Care must be taken to ensure adequate ventilation and respiratory and metabolic acidosis should be promptly corrected. Sympathetic activation or noxious stimuli can also precipitate an acute increase in PVR. The most vulnerable times are during intubation, tracheal and pharyngeal suctioning, surgical stimulation, and emergence from anesthesia. Blunting sympathetic responses with sufficient anesthetic depth and the use of narcotics can help attenuate increases in PVR.

Because a PH crisis is a cycle revolving around RV failure, disturbances at any point in the cycle which contribute to RV failure can trigger a crisis. A decrease in SVR, which often accompanies anesthetic induction, can lead to hypotension and coronary ischemia. Volatile anesthetics and certain IV induction agents can also cause direct myocardial depression. While hypovolemia can contribute to inadequate preload and

cardiac output, RV dysfunction from overdistension may also decrease LV preload. All of these mechanisms may contribute to or exacerbate a PH crisis.

What are the impending signs of a PH crisis?

Impending signs of a PH crisis include hypotension, hypoxemia, decreased end-tidal CO_2 , and changes in heart rate. Bradycardia is often observed and is an ominous sign. Signs of RV strain, such as ST depression or T-wave inversion in the right precordial or inferior leads, may be seen on ECG. The onset of a PH crisis can be gradual, with a slow decline in blood pressure and oxygen saturation. However, a PH crisis can also be sudden, with complete cardiovascular collapse. It is important to be extremely vigilant and treat hemodynamic changes promptly because if the cycle ends in cardiac arrest the resuscitative outcomes in this population are poor.

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Signs of impending PH crisis include hypotension, hypoxemia, decreased end-tidal CO_2 , and bradycardia. Signs of RV strain, such as ST depression or T-wave inversion in the right precordial or inferior leads, may be seen on ECG.

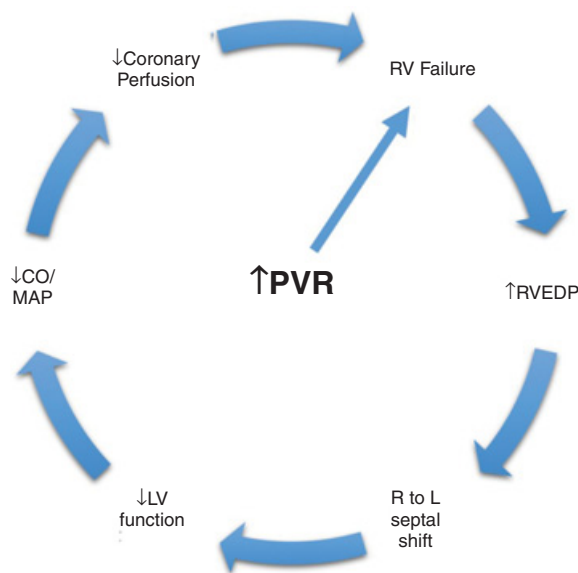


Figure 40.1 The cycle of a pulmonary hypertensive crisis. CO, cardiac output; MAP, mean arterial pressure; PVR, pulmonary vascular resistance; RVEDP, right ventricular end-diastolic pressure.

How should a PH crisis be treated?

The aims in treating a PH crisis are to support CO and coronary perfusion while taking measures to decrease PVR and augment SVR. (See Table 40.2.)

Decrease PVR

- Ensure delivery of 100% oxygen and institute mild hyperventilation.
- Make sure the patient is warm and correct metabolic or respiratory acidosis.
- Ensure adequate analgesia to decrease sympathetically mediated increases in PVR.
- Inhaled nitric oxide, administered within a range of 20–80 ppm, is the pulmonary vasodilator of choice for acute PH crisis, as it selectively and rapidly dilates the pulmonary vasculature without decreasing SVR. Abruptly stopping iNO can lead to rebound PH, so once started iNO should be slowly titrated off.

Increase SVR

- Vasopressors should be started to maintain and/or increase SVR. It is essential to preserve coronary perfusion and maximize oxygen delivery to the deteriorating RV by increasing SVR.

Table 40.2 Treatment of a Pulmonary Hypertensive Crisis

Goal	Therapy
Decrease PVR	100% Oxygen Nitric oxide Increase anesthetic depth Correct respiratory acidosis <i>Mild hyperventilation</i> Correct metabolic acidosis <i>Sodium bicarbonate</i>
Increase SVR	Vasopressors <i>Phenylephrine</i> <i>Vasopressin</i> <i>Norepinephrine</i>
Support CO	Judicious fluid resuscitation Inotropes <i>Epinephrine</i> <i>Dopamine</i> <i>Dobutamine</i> ECLS/ECMO

ECLS, extracorporeal life support; ECMO, extracorporeal membrane oxygenation; iNO, inhaled nitric oxide; PVR, pulmonary vascular resistance; SVR, systemic vascular resistance.

- Vasopressin lowers PVR while increasing SVR, making it an attractive choice.
- β -Agonist effects of norepinephrine add the advantage of inotropic support.
- Phenylephrine, often more easily obtained, can also be safely used.

Support CO

- A fluid bolus can be considered to ensure adequate preload and support CO, but RV distension should be avoided, especially with severe RV failure.
- Epinephrine, dopamine, or dobutamine can all be used for support of CO, though the tachycardia caused by these agents can worsen ventricular filling and increase myocardial oxygen consumption.
- Milrinone, in addition to its inotropic and lusitropic properties, is also a pulmonary vasodilator. However, the accompanying decrease in SVR often limits its utility and this medication is best avoided during a PH crisis.
- If cardiac arrest occurs, extracorporeal life support (ECLS, ECMO) should be initiated early.

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Milrinone, in addition to its inotropic and lusitropic properties, is also a pulmonary vasodilator and can seem like an attractive choice. However, the accompanying decrease in SVR often limits its utility and this medication is best avoided during a PH crisis.

What medications should be prepared for a patient with PH?

Resuscitation medications, including epinephrine and phenylephrine, should be immediately available. For higher risk patients, inotropic and vasopressor infusions should be prepared. Immediate availability of iNO is often prudent. In the highest risk patients, instituting “ECMO standby,” or having a team available to initiate ECMO should decompensation occur is advisable.

Should invasive or advanced monitors be utilized?

The decision to use invasive monitoring depends on the severity of the patient’s PH as well as the complexity of the case. Arterial access is often advantageous, as it facilitates close monitoring of hypotension, hypercarbia, or acidosis, all of which can trigger a PH crisis. Central venous access may be necessary for the administration of vasoactive medications and can serve as a guide to monitor preload through observation of central venous pressure trends. Transthoracic or transesophageal echocardiography can also provide valuable real-time information about the function and filling of the RV.

Is it safe to premedicate patients with PH?

Premedication carries both risks and benefits. In an anxious child sedation can prove beneficial by alleviating the increase in PVR and myocardial oxygen consumption caused by catecholamine surges. However, oversedation can result in hypoventilation, hypercarbia, and hypoxia, which may increase PVR. Therefore, if premedication is used, the patient should be closely monitored.

Is general anesthesia indicated for PICC line placement in this patient?

Placement of a PICC line is typically not a painful procedure; therefore, general anesthesia is usually not indicated. However, if a patient proves uncooperative or unsafe for sedation or monitored anesthesia care, a deeper level of sedation or anesthesia may be indicated.

What type of anesthetic induction could be performed on this child?

While general anesthesia is unlikely to be required in a developmentally normal 10-year-old patient for PICC line placement, this patient would likely require anxiolysis during the procedure. Slow titration of an anxiolytic, such as midazolam, is indicated to ensure cooperation while

maintaining adequate ventilation. Anxiolysis with other medications, such as dexmedetomidine and ketamine, may also prove effective. Caution is advised with the use of dexmedetomidine in patients with untreated PH, as concern exists for sudden increases in PVR with bolus administration in children.

How do anesthetic medications affect patients with PH?

Volatile Agents

Volatile agents cause a dose-dependent depression of myocardial contractility and SVR. On the other hand, they also attenuate hypoxic pulmonary vasoconstriction and cause a small amount of pulmonary vasodilation, lowering PVR. These agents are generally well tolerated for anesthetic maintenance in patients with PH. Though not well studied, nitrous oxide appears to have minimal effects on PVR in infants and children. Its use may be limited if the patient is unable to tolerate an FiO_2 of $<100\%$.

Intravenous Agents

Propofol causes a significant reduction in SVR, necessitating caution with its use as a bolus medication in patients with moderate to severe PH. However, the combination of propofol and ketamine administered as an infusion has been successfully utilized in patients with PH.

Ketamine increases SVR and maintains blood pressure with minimal to no change in PVR, making it a useful medication for patients with PH. Recent studies demonstrate its use is well tolerated in children with PH and may even lower PVR.

Etomidate has a favorable cardiovascular profile with minimal to no effects on contractility, mean arterial blood pressure and SVR, making it an appropriate agent for induction in patients with PH. Studies are inconsistent regarding effects on PVR.

Dexmedetomidine can serve as a useful adjunct to an anesthetic by providing sedation, anxiolysis, and analgesia while avoiding significant respiratory depression. It has no effect on PAP or PVR and can transiently increase SVR. However, dexmedetomidine may also decrease heart rate, which may not be well tolerated in a patient with impaired ventricular function. This decrease in heart rate can be attenuated by using a bolus dose of 0.5–1 mcg/kg administered slowly over 10–15 minutes. Additional caution is advised when medications, such as digoxin, are part of the child's medication regimen, as the combination may result in profound bradycardia.

Opioids have a very stable hemodynamic profile and blunt the effects of noxious stimuli, making them a vital

part of the anesthetic plan. Bradycardia may also occur with opioid administration. Care must be taken with long-acting opioids if extubation is planned, as they can lead to hypoventilation, hypercarbia, and hypoxia.

Midazolam also has minimal hemodynamic effects and can be useful in patients with PH. When used as premedication for anxiolysis patients should be carefully monitored, as hypoventilation may occur, especially in patients with upper airway disease.

How can general anesthesia be induced in patients with PH?

Slow IV titration of lower doses of several drugs can achieve adequate anesthetic depth without incurring the marked hemodynamic changes associated with high doses of a single drug. Inhalational induction of anesthesia will be tolerated only in patients with very mild forms of PH. An IV induction is recommended for patients with moderate to severe PH using medications with minimal hemodynamic effects such as etomidate and ketamine, supplemented with opioids and/or midazolam. For the highest risk patients, a slow induction with a propofol–ketamine infusion, as described earlier, may be utilized, in addition to a phenylephrine infusion to maintain SVR. In these patients, if feasible, blood pressure monitoring via an arterial line during induction is advisable.

What airway management methods are appropriate?

The incidence of anesthetic complications in this population has not been shown to correlate with the type of airway used. Sympathetic stimulation caused by insertion of an endotracheal tube (ETT) or laryngeal mask airway (LMA) must be mitigated by adequate depth of anesthesia, opioid use and/or airway topicalization. The use of muscle relaxants to avoid coughing and enhance the ability to control ventilation offers advantages in most procedures. The use of an LMA, when appropriate, is often less stimulating than an endotracheal tube. A natural airway, if appropriate, has the advantage of avoiding airway instrumentation; however, the risks of hypoventilation and hypercarbia necessitate a high level of vigilance.

What ventilatory concerns exist in patients with PH?

Ventilation strategies to decrease PVR should be employed, with avoidance of hypercarbia. Physiologic levels of positive end-expiratory pressure (PEEP) and

tidal volumes at functional residual capacity should be used to prevent atelectasis, which leads to ventilation-perfusion mismatch. High PEEP and/or high peak inspiratory pressures, excessive tidal volumes, and long inspiratory times overdistend alveoli and compress alveolar capillaries. This combination leads to decreased venous return and increased PVR and should be avoided. Supplemental levels of inspired oxygen should be used as needed to avoid hypoxemia.

How should fluid management be approached in this population?

Patients with PH typically have a stiff RV that requires an elevated central venous pressure to maintain filling volumes and forward flow. However, overadministration of fluid can distend the RV, negatively impacting contractility. Resuscitative fluids should be given judiciously and slowly with time to allow equilibration while avoiding any rapid or major fluid shifts. If RV function is at all compromised, the use of inotropes and vasopressors should be initiated early to minimize the amount of fluid administered to maintain CO.

What precautions are necessary during emergence from anesthesia?

Emergence from anesthesia is perhaps even more risky than induction in patients with PH as it can be less well controlled. Increases in PVR can occur with coughing or bucking, inadequate pain control, and tracheal suctioning. Suctioning should take place during a deeper level of anesthesia and the use of opioids to limit sympathetic stimulation can also help minimize risk. In some patients extubation to noninvasive positive airway pressure or high-flow nasal cannula may be advisable.

Clinical Pearl

Emergence from anesthesia is perhaps even more risky than induction in patients with PH as it can be less well controlled. Suctioning during a deeper level of anesthesia and the use of opioids to limit sympathetic stimulation will help minimize risk.

What should the postoperative care of the patient include?

The increased risk of morbidity and mortality associated with anesthesia in the PH patient continues in the recovery room. Continuous monitoring with prompt recognition and treatment of symptoms is imperative. Either splinting due to inadequate pain control or the excessive use of narcotics can lead to hypoventilation and hypercarbia. Nausea, vomiting, and fluid underresuscitation may lead to dehydration and inadequate preload. Pain or postoperative delirium can cause a sympathetic surge. High-risk patients, or those who had any significant intraoperative events, should be admitted to the intensive care unit immediately following surgery. Outpatient surgery should be considered only for the lowest risk patients who undergo uneventful anesthetics, recover completely to baseline status, and are able to resume all preoperative medications.

Suggested Reading

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