Pulmonary Hypertension Crisis: An unexpected challenge

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Introduction

Although the incidence of pulmonary hypertension is only 2.4 per million adults and is unknown in children, it is a diagnosis that carries significant morbidity and mortality. Pulmonary arterial hypertension (PAH) can present at any age and has multiple different causes which all ultimately lead to elevated pulmonary arterial pressures.

The overarching disease progression can be thought of in the following manner: pulmonary arteriole dysfunction (some combination of endothelial dysfunction/proliferation, vasoreactivity, and thrombosis) leads to progressive elevations in pulmonary vascular resistance and arterial pressures which lead to right heart failure and eventually death.

The current definition of PAH requires a mean pulmonary arterial pressure >25mmHg at rest and a pulmonary vascular resistance index of > 3 Wood units/m^{2}..

We will discuss the management of a patient who had an unexpected pulmonary hypertensive crisis in the cath lab.

Case Report

A 2yo former 36 week infant with dTGA with IVS (s/p ASO), bronchomalacia with collapse of left mainstem bronchus and possible PAH of unknown origin presented for bronchoscopy and aortopexy vs external bronchial stent. The patient had an aborted procedure 3 months prior due to desaturation after induction to 70% without recovery requiring intubation for 3 weeks. At that time he was found to be positive for viral and bacterial infections. He was discharged on no PAH medications. No recent echos were available.

The patient was brought to the OR, standard ASA monitors + NIRS were applied and underwent an uneventful inhaled induction with sevoflurane and IV placement. Titrated doses of propofol (< 1 mg/kg) were administered when the airway was turned over to ENT for bronchoscopy. During bronchoscopy, the anesthesia team was placing a radial arterial line and could no longer palpate a radial pulse. NIBP showed a drop in SBP from 80mmHg to 30mmHG with minimal anesthetic. He required epinephrine x 2 doses (1mcg/kg), but returned to baseline quickly and the airway was secured. A few minutes after recovering, his blood pressure dropped again, this time requiring CPR x 8 min for hypotension, but fully recovered once again on epinephrine infusion. The patient continued to have recurring intermittent hypoxia and further surgery was aborted. He was kept in the OR for management of presumed PAH with a severely dilated RV on echo. His therapy consisted of escalating doses of epinephrine and milrinone infusions, NO administration, IV sildenafil boluses, an epoprostenol infusion (Valetri®), and inhaled iloprost via ultrasonic nebulizer. Intraoperative consultation with his treating pulmonologist helped guide his therapy. The patient was transferred intubated to the ICU. He persisted with intermittent desaturations due to severe episodes of PAH crises in the ICU despite escalating dosages but was ultimately extubated after 16 days and discharged home on PAH medications.

Anesthetic Principles for PAH

- Components of PH crisis

- Increase in PVR -> increased RV afterload -> increased RV wall stress -> RV dilation -> decreased coronary perfusion -> LV/RV ischemia -> cycle perpetuates

- Potential triggers:

- Hypoxia, hypercarbia, acidosis, sympathetic surge (pain/agitation), coughing/suctioning

- Commonly used techniques to decrease PVR

- 100% FiO2, Hyperventilation, correct acidosis, prevent/treat pain and agitation, decrease mean airway pressures

- Other things to consider:

- Maintain/support systemic pressure: required to overcome elevated PA pressures
- If you think that patient is having a PH crisis, do all of the above, treat potential underlying causes and start to consider pulmonary vasodilators as well as potential for ECMO

Common Medication Pathways

Class	Nitrous oxide pathway	Prostacyclin pathway	Endothelin pathway
Medications	- Inhaled NO - PDE5 inhibitors - Sildenafil - Tadalafil	- Epoprostenol - Iloprost -Treprostinil	- Bosentan - Ambrisentan
Mechanism of Action	- NO- increases available NO -> activates soluble guanylyl cyclase -> inc conversion of GTP to cGMP - PDE5 inhibition -> inhibits conversion of cGMP to GMP -> inc cGMP	- Act as prostacyclin analogs -> bind I-prostanoid receptor -> activation of adenylyl cylase -> inc conversion of ATP to cAMP	- Act as Endothelin- 1 receptor antagonists
End result	Increased cGMP -> activation of protein kinase G -> vasodilation and decreased vascular proliferation	Increased cAMP -> activation of protein kinase A -> vasodilation and decreased vascular proliferation	Prevent endothelin A and B receptor activation -> prevention of vasoconstriction and proliferation

Intra-operative Use of Medications

Oral:
- Sildenafil: starting 0.5mg/kg TID -> maintenance 1 mg/kg TID - average dose 10-20mg TID
- Tadalafil: 1 mg/kg/d - once daily dosing
- Bosentan: 2 mg/kg BID
- Ambrisentan: 2.5-10mg daily

Inhaled:
- Nitric Oxide: connects directly to circuit, requires NO tank/delivery system
  - Dose: 5-40ppm (commonly started at 20ppm)
- Iloprost: requires ultrasonic nebulizer to be integrated into circuit
  - 2.5 mcg 6-9 times/day up to 5mcg 6-9 times/day
- Treprostinil: 3 breaths (18mcg) QID

IV:
- Sildenafil: 0.4mg over 3hrs or 1.6 mg/kg/day (continuous)
- Epoprostenol: 1-3 ng/kg/min uptitrated to 50-80 ng/kg/min
- Treprostinil (can be given subQ): 1.25-2 ng/kg/min up to 50-80 ng/kg/min

Discussion

Though uncommon, this case illustrates the multi-modal treatment options now available in anesthetizing locations. PAH crises typically present with hypotension, hypoxia and subsequent cardiac arrest if not treated quickly. Initial therapy includes increasing FiO2, slight hyperventilation, deepening of the anesthetic, inhaled NO, and milrinone and epinephrine infusion to support the RV. Novel therapies include targeted pulmonary arterial vasodilation through the use of calcium channel blockers, and the NO, endothelin and prostacyclin pathways. We approached the crisis that occurred in our patient by using IV sildenafil (a PDE-5 inhibitor), IV epoprostenol (Valetri®) and inhaled Iloprost ® (prostacyclin analogs). The addition of these medications in the intra-operative setting may soon be playing a much larger role in our practices as we see more patients with PAH in the pediatric setting. Of note, Valetri® is ultra-short acting and requires a dedicated intravenous line with a second site available at all times while inhaled Iloprost ® requires a specialized ultrasonic nebulizer not routinely available in the OR.

REFERENCES

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