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She Was Advised Not to Get Pregnant and She Did: Pulmonary Hypertension and Pregnancy

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Stem Case and Key Questions Content

You are called to see a 25 year old G1 P0 patient who is 20 weeks pregnant and just admitted to the ICU with known pulmonary hypertension (PH). She was counseled not to get pregnant by both her pulmonologist and cardiologist and therefore was reluctant to seek pre-natal care. She was hospitalized today after showing up for her first obstetrical appointment.

What are the diagnostic criteria for PH? What is the rate of morbidity and mortality in a pregnancy for a patient with PH? How common is this disease process?

She made this appointment after having worsening dyspnea over the last few days. At the time of her diagnosis she was told she had pre-capillary PH with mean pulmonary artery pressure (mPAP)=55, right atrial pressure (RAP)=12, right ventricular ejection fraction (RVEF)= 30%, pulmonary capillary wedge pressure (PCWP) = 8, cardiac index (CI) = 2.2

What are the normal values for central venous pressure (CVP), RAP, PAP, PCWP, left atrial pressure (LAP)? What is the difference between pre- and post-capillary PH? What are the common etiologies of the two major causes? What right heart catheterization values would you expect in someone who has pre-capillary PH? Post-capillary PH? What kind of symptoms would a patient with PH have?

She had been diagnosed with idiopathic PH and had been on bosentan and sildenafil and remained stable with World Health Organization (WHO) class III symptoms for 18 months prior to pregnancy.

What drugs are used for treatment of PH and how do they work? What other “supportive therapy” should be considered in patients with PH? What additional drugs will she likely be placed on in the hospital?

On admission to the ICU her BP=115/54 SaO2= 91% on 6L FM, RR=20, HR=87. She is started on epoprostenil IV with improvement in her SaO2 to 95%. You get called to a cesarean section as the obstetrician and ICU attending are heatedly discussing whether to give this patient furosemide.

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Explain why hypovolemia can be extremely detrimental to a patient with RV failure. Explain why overloading the right heart with volume can be extremely detrimental to a patient with RV failure.

The plan is to keep the patient in the hospital until delivery. At 27 5/7 weeks she will receive 48 hours of betamethasone treatment and have an elective cesarean section at 28 weeks gestation. You are called to get consent for the anesthesia.

How openly would you discuss the patient's risks of mortality with her? Would you include the family in the discussion? Does the fact that there are no alternatives to having a high risk procedure and anesthetic make a difference? Does the fact that her risk of mortality is related to delivering the baby rather than directly to the anesthetic make a difference? Is an elective cesarean section safer than a normal spontaneous vaginal delivery (NSVD)?

24 hours before the scheduled c-section the patient ruptures her membranes but does not go into labor. The obstetricians decide not to change her scheduled c-section time so she can complete her course of betamethasone, her anticoagulation can be stopped and her prostanoids can be changed from IV to inhalation.

What kind of anesthetic will you give her? What are the advantages and disadvantages of GA? Of neuraxial anesthesia? What are some of your goals during the anesthetic to promote right ventricular function? Would you place a CVP catheter in this patient to help guide treatment? A PAC? Would echocardiography be helpful?

2 hours before the scheduled c-section the patient spikes a fever to 101 F. Her HR increases slightly but she remains stable. Her temperature comes down with acetaminophen and she is treated with ampicillin and gentamycin for chorioamnionitis.

Would you still consider placing an epidural in this patient with chorioamnionitis? How about a patient without her co-exiting disease but a diagnosis of chorioamnionitis? Would you place an epidural in a patient with a fever of unknown origin? A patient with presumed chorioamnionitis whose fever was 101.7 after acetaminophen?

You place an epidural and bolus her with 0.5% bupivacaine slowly. She has a good T4 level after 40 minutes and remains stable prior to delivery of the baby. Within 5 minutes of delivery of the baby the BP falls to 82/40 and her oxygen saturation falls from 94% on 6L to 88%.

What is happening? What is the optimum way of treating this?

Model Discussion Content

Pulmonary hypertension (PH) is a rare yet devastating disease process. It's incidence in the United States is 2-5/million/year. In normal patients the pulmonary arterial complex is highly compliant with low resistance to allow for high flow. The system can recruit or close arteries as cardiac output changes. In patients with pulmonary hypertension remodeling of the pulmonary vasculature, with loss of cross sectional area, leads to increased pulmonary vascular resistance that culminates in right heart failure and death.[1] The most recent review of the literature shows a

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mortality rate for idiopathic PH in pregnancy at 17%, but the mortality remains between 28-33% in pregnant patients with PH due to congenital heart disease and other causes.[4] Diagnosis is made with right heart catheterization. The severity of PH is quantified by the elevation in mPAP with mild 25-40 mmHg, moderate 41-55 mmHg and severe >55 mmHg.

Pre-capillary PH is caused by high resistance in the pulmonary vascular bed leading to high pulmonary artery pressures(PAP). Post- capillary PH is caused by left heart problems including congenital heart disease and left heart failure, leading to high PAPs. Right heart catheterization will differentiate between pre- and post- capillary PH by the measurement of left atrial pressure (LAP) that is transmitted back to pulmonary capillary wedge pressure (PCWP). If LAP is > 12 (and therefore PCWP is >12 mmHg) then left heart pathology is involved. Transpulmonary gradient, TPG, (mPAP-LAP) is also considered.[2] See normal values, values that would lead to a diagnosis of PH and example patient values below.

Table 1

	Normal	Pre-capillary PH		Post-capillary PH	
		Diagnosis	Example	Diagnosis	Example
s PAP	25		84		52
dPAP	10		46		34
mPAP	15	>25	58	>25	40
mRAP	2-5		15		16
CVP	3-8		15		16
PCWP	7	<15	8	>15	29
mLAP	7		8		29
TPG (mPAP –LAP)	8	>12	51	<12	11
PVR	20-120	>240	1120	<240	183
CO	6		3.5		3.0

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Table2

Causes Pulmonary Hypertension

Abbreviated list

Pre-capillary PH Causes

- Idiopathic PH
- Heritable
- Connective tissue disease
- Lung disease
- Chronic hypoxia
  - OSA
  - COPD
  - Restrictive
- Chronic TE

Post-capillary PH

- Left Heart Disease
  - Systolic dysfunction
  - Diastolic dysfunction
  - Valvular dysfunction

Signs and symptoms associated with PH include: dyspnea, fatigue, dizziness, syncope, chest pain, palpitation, orthopnea, edema, cough, ascites and hepatomegaly.
The common drugs used in patients with PH and their pharmacology are listed in Table 3 below.

Table3

Medications used in PH

Type	Mode of Action	Specific	Route	Notes
Calcium Channel Blocker	Blocks calcium into cells, decreasing ADP associated vasoconstriction	Nifedapine Diltiazem Amlodipine	Oral Oral Oral	Only effective in a small % of patients with Pre-capillary PH
Prostanoid	Promotes production of cAMP leading to vasodilitation	Epoprostenol Treprostinil Iloprost	IV SQ/IV Inhaled	IV form interferes with platelet aggregation. Very short half lives
Endothelin Receptor Antagonists	Blocks endothelin, a potent vasocontrictor	Bosentan Ambrisentan	Oral Oral	Hepatotoxic
Phosphodiesterase Type-5 Inhibitors	Blocks phosphodiesterases from breaking down cGMP, a vasodilator	Sildenafil Tadalafil	Oral Oral	
Nitric Oxide	Promotes procuction of cGMP, a vasodilator	Nitric oxide	inhaled	

3

All patients with PH should be treated with oxygen. It has been shown to decrease pulmonary vascular resistance (PVR) in patients with pre-capillary PH. Diuretics may be helpful for a

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dilated right ventricle. However, caution must be taken not to decrease pre-load below optimal diastolic filling. Unless contraindicated, patients with PH should be anticoagulated to prevent thromboembolic events.[1] They are much more sensitive to the deficits created by pulmonary emboli and the inflammatory reaction that it may bring about.

In a patient with PH right ventricular cardiac output (CO) is precarious. Decreasing intravascular volume to the point where diastolic filling does not optimize fiber length can result in decreased inotropy and decreased ejection fraction (EF). As EF decreases the right ventricle may dilate. Right ventricular dilatation with intraventricular septal shift is extremely hazardous. This can be caused by an increase in PVR, a decrease in right ventricular function or an increase in intravascular volume. As the septum bows into the left ventricle it loses its stability leading to even lower right and left ventricular EF, it creates unfavorable right ventricular fiber direction and it increases tricuspid regurgitation (TR) through annular stretch. This scenario can lead to the frequently lethal *acute decompensated right heart failure (ADRH).*[2]

Anesthesiologists are required to give a procedural description, potential risks, benefits, complications and alternate options during informed consent.[5] The level of disclosure about the amount or risk is not well defined. In the “reasonable person standard” physicians are required to disclose information that a reasonable person would need to make a decision about the procedure. There is also the “subjective person standard” where the physician determines the individual patient’s wants and needs about risk disclosure. This is difficult to use as a legal standard but is considered the ideal level of disclosure. In the subjective person standard a physician may not discuss the risk of death if it is clear that the patient would not benefit from the disclosure.[6] Patients having no alternative to the high-risk undertaking of delivering the baby represent a very unique situation. Ideally, the cardiologist of a patient with severe PH would fully disclose the risks prior to the patient’s pregnancy and by becoming pregnant the patient has consented to those risks.

Mortality is high in both NSVD and cesarean section in patients with PH. Increasingly, case reports are describing elective cesarean section as the mode of delivery. NSVD has less bleeding, less fluid shifts and a lower infection risk. However, the unpredictability and uncontrolled quality of spontaneous vaginal delivery make it difficult.[7] General anesthesia is complicated by increases in PVR from positive pressure ventilation and PEEP, decreases in cardiac contractility caused by inhalation agents, and sympathetic responses to induction and intubation. Titration of an epidural can provide hemodynamic stability. However, there is always a risk of decreased MAP and increased heart rate that could be catastrophic in a patient with severe PH. Below is a table describing the anesthetics goals to maintain RV function.
Patients with severe PH need to have invasive monitoring during a cesarean section. An arterial line and central venous pressure monitoring would be necessary. Pulmonary arterial catheter placement carries high risk in these patients. They are prone to PA rupture, thrombosis and any arrhythmia initiated by the placement could lead to acute decompensated right heart failure (ADRHF).[8] Cardiac output measurement and therefore response to fluid boluses, pressor therapy or inotropes, is difficult to measure in these patients. Pulmonary regurgitation will cause

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thermodilution CO's to be overestimated when low and underestimated when high. Echocardiography is very useful in that it can give an assessment of fluid volume, right heart function, TR, and degree of right heart dilatation. A central venous pressure line can be used to measure mixed venous oxygen saturation and RAP which can be helpful in guiding therapy. CVP monitoring will be accurate but is a late sign during right heart failure. Cardiac output could also be monitored by pulse contour cardiac output.

Choriomnionitis in the parturient is common affecting 1-3% of patients with 8% of those having bacteremia. [9] However, the rate of CNS infection, meningitis or epidural abscess, is extremely rare in general and even less likely in the obstetrical population. The decreased rate in parturients may be due to the relatively short duration of catheter use, the lack of immunocompromised patients or the bacteriostatic effects of local anesthetics. No study has linked dural puncture in a patient with bacteremia to development of a CNS infection.[10]Experts recommend using clinical judgment in each case when deciding if the risks outweigh the benefits of neuraxial anesthesia or analgesia in the face of infection. They suggest a spinal or epidural can be safely given to a patient with a systemic infection who is appropriately treated with antibiotics and has shown a response to treatment. [11] These patients should have diligent follow up, as even a short delay in diagnosis of a CNS infection can lead to worsened outcomes. It should be remembered that most cases of meningitis and epidural abscess occur spontaneously.

Acute decompensated right heart failure (ADRHF) on a chronically impaired right heart from PH occurs frequently perioperatively and is the common cause of mortality. Usually the acute precipitating event is preventable. However, in this case it is likely brought about by the autotransfusion at the time of birth. Oxytocin administration and decompression of the IVC could also have contributed to the acute decompensation. Table 4 lists many of the factors that can be controlled to prevent ADRHF intra- and post-operatively. As discussed above when the right heart begins to fail and the intraventricular septum flattens the left heart function is reduced leading to a decrease MAP. This rapidly can become a lethal cycle. During ADRHF as MAP falls and venous pressure increases severe reductions in organ perfusion pressures occur, including right coronary artery perfusion, and quickly lead to multi-organ system failure.

Treatment of ADRHF is extremely difficult since many of the drugs that may improve right heart function (phosphodiesterase inhibitors, calcium sensitizers) lead to further systemic hypotension. Goals of treatment include control of cardiac rate and rhythm, optimization of RV filling (described above), improvement of RV function, aggressive treatment of systemic hypotension and reduction of PVR[1]. Case reports in pregnant patients[12] as well as non-pregnant patients have suggested that vasopressin may cause less increase in PVR with maintenance of systolic blood pressure. Milrinone, a phophodiesterase inhibitor, is a powerful ionotrope but also causes vasodilatation. It has been used successfully in combination with dobutamine. Inhaled prostacyclins or nitrous oxide should also be administered to help decrease PVR. IV prostacyclins may also be used in the setting of ADRHF.

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Anesthetic Goals for Pulmonary Hypertension

Pulmonary Vasodilitation
• Adequate anesthetic depth at induction/intubation to avoid activation of the SNS
• Improved FiO2
  ○ Supplemental Oxygen
  ○ Normothermia to avoid decrease in HPV
• Optimal ventilatory volume
  ○ High volume – capillary compression
  ○ Low volume -- hypoxia, hypercarbia causing vasoconstriction
• Permissive Hypocapnia (PaCO2 <30-35 mmHg)
• Alkalosis (pH>7.4)
• Maintain adequate levels of anesthesia – avoid activation of SNS
• Avoid shivering – causes increase PVR
• Adequate pain management – avoid activation of SNS

Decrease RV Afterload
• Maintain spontaneous respiration
• Neutral Position
  ○ Flat to Reverse Trendelenburg
  ○ Supine
• Minimize PEEP
• Minimize compression effects of surgery
  ○ Avoid pneumoperitoneum
  ○ Avoid compression of intrathoracic structures
• Avoid or anticipate pulmonary emboli – DE-AIR, common in joint replacement and c-section

Maintain RV Function • Minimize inhalation anesthetics • Avoid high doses of propofol and etomidate • Treat anemia – increases RV work • Euvolemia • Quick treatment of arrhythmias • Avoid tachycardia
Avoid Systemic Hypotension • Avoid heavy and high regional anesthesia/analgesia • Use oxytocin with caution

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