Acute Thrombosis of Mechanical Valve for Emergency Redo AVR. By the Way, the Patient Is Pregnant!

Learning Objectives:
At the end of this discussion the participant will be able to:
1. Understand anticoagulation for mechanical prosthetic valves.
2. Understand the mechanism of action and teratogenic effects of warfarin.
3. Understand the warnings and precautions of enoxaparin use in pregnant patients.
4. Understand systolic blood pressure requirements for adequate placental blood flow.
5. Understand the implications of cardiopulmonary bypass in a pregnant patient.
6. Understand the effects of epinephrine, phenylephrine, norepinephrine, and vasopressin on uterine and placental blood flow.

PBLD:

STEM CASE - KEY QUESTIONS
This patient is a 28 year old, healthy female, who was born with a bicuspid aortic valve. At age 24, she underwent an aortic valve replacement with a 21mm St. Jude mechanical prosthetic valve for severe aortic insufficiency without complication. She was maintained on warfarin until recently when she electively decided to become pregnant. Warfarin was discontinued and therapy with enoxaparin was initiated by her obstetrician. A recent ultrasound showed a normally developing fetus at 23 weeks gestation.

Questions:
1. Why was the patient on warfarin? At what level is the INR maintained for mechanical aortic valves?
2. Why was the warfarin discontinued when she became pregnant?
3. Was enoxaparin a good choice for replacement therapy? Are there any alternatives?

She presented to the emergency room at 23 weeks gestation with chest pain and shortness of breath, worsening throughout the evening. CXR showed pulmonary infiltrates and an enlarged cardiac silhouette. Her workup included a transthoracic echocardiogram which showed almost complete occlusion of the prosthetic aortic valve with left ventricular distention. During her evaluation she became more short of breath and began to show decreased alertness, and her blood pressure decreased to 90 mmHg. Labs were all within normal range, with PT elevated at 15.1 sec. An obstetric ultrasound showed a normal, active fetus with a fetal heart rate of 140-150, with good beat-to-beat variability.
Further decompensation occurred in the emergency room, and cardiothoracic surgery was consulted emergently, who then consulted the cardiac anesthesiologist. The patient had an arterial line placed and maintained an arterial blood pressure in the 80-90mmHg range. By the time the anesthesiologist and surgeon arrived, she was sitting upright, gasping for breath. The patient was rushed emergently to the operating room for redo aortic valve replacement using cardiopulmonary bypass.

Questions:
4. What is the optimal systolic blood pressure to ensure adequate placental blood flow?
5. What are the implications of using cardiopulmonary bypass in a pregnant patient? What is the incidence of fetal demise during maternal cardiopulmonary bypass?

In the operating room, EKG, pulse oximeter, and peripheral i.v. were placed. Her arterial blood pressure was 60/40 and the patient was in extremis. Since the patient could not lie flat, a central line could not be placed prior to induction. OB/GYN was called to monitor the fetus during the surgery. They recommended an emergency C-section. However, it was thought the patient needed immediate replacement of her aortic valve prosthesis and would not tolerate a C-section. The patient was given 30 ml bicitra, and a rapid sequence induction was accomplished with 14 mg of tomidate, 100 mg of succinylcholine, 1 mg of midazolam, and 150 mcg of fentanyl, while applying cricoid pressure until the trachea was successfully intubated. Blood pressure immediately following induction was 65/45. 20 mcg of epinephrine were given peripherally. Her blood pressure improved to 75/50.

Questions:
6. Was a rapid sequence induction indicated?
7. Was this the best choice of induction agents?
8. Should the obstetricians have been allowed to proceed with the C-section? What is the survival rate of a pre-term infant at 23 weeks gestation?

The patient was placed in Trendelenberg position for central line placement. Within seconds, she became extremely hemodynamically unstable with blood pressure 40/25. Central line attempt abandoned. The obstetric nurse arrived and asked to be allowed to place the external fetal monitor on the abdomen but was refused because of the patient’s instability. 100 mcg epinephrine were given without response. The blood pressure continued to fall to a systolic of 25mmHg, so chest compressions were begun to help ensure adequate blood flow. The surgeons emergently prepped the chest, draped, and made incision followed immediately by sternotomy, with intermittent chest compressions continuing, and epinephrine boluses given at 1 minute intervals.

Questions:
9. Why did the patient become more hemodynamically unstable?
10. Was the choice to do chest compressions correct? Were there alternatives?
11. Should the central line attempt have been abandoned?
12. Should the obstetric nurse have been allowed to place the fetal monitor?

The patient was heparinized and emergently cannulated. A TEE probe was passed without complication and a quick exam showed a mechanical prothesis with non-mobile leaflets stuck in the almost closed position, a distended left ventricle, and a left ventricular ejection fraction of 5%. Cardiopulmonary bypass was instituted after heparinization. Bypass flows were kept high at 6 L/min, and the mean blood pressure was maintained high at 90-100mmHg.

Questions:
13. Why were bypass flows and mean arterial blood pressure kept high?
14. Should the anesthesiologist have taken the time for TEE placement and exam?

The valve replacement was completed without complication. Upon weaning from cardiopulmonary bypass, a TEE showed improved myocardial function with an LVEF 30% and no segmental wall motion abnormalities on 0.1 mcg/kg/min epinephrine. However, the arterial blood pressure could not be maintained above 70mmHg. Increase of the epinephrine infusion rate caused ventricular dysrhythmias. A decision was made to initiate norepinephrine at 0.05 mcg/kg/min. The obstetricians were furious! However, the arterial blood pressure increased to 110/65 and the remainder of the case was uneventful.

Questions:
15. What is the reason for the decreased blood pressure after CPB?
16. Should norepinephrine be used in a pregnant patient? What about epinephrine? What about vasopressin?

An ultrasound at the end of the case showed a fetus with a fetal heart rate in the 120's. The patient carried the fetus to term and delivered a normal, healthy baby boy four months later.

**PROBLEM BASED LEARNING DISCUSSION**

All patients with mechanical prosthetic valves must be anticoagulated to prevent thrombus formation and subsequent embolic events. With a St. Jude mechanical valve in the aortic position, the incidence of stroke is 0.2-3% per year, even with "adequate" anticoagulation. A mechanical prosthetic valve in the mitral position has a slightly higher rate of thrombus formation. Therefore, it is recommended that the INR be kept >3.0 for aortic valves and >3.5 for mitral valves.

Warfarin is an orally active 4-hydroxycoumarin whose effect is due to inhibition of the γ-carboxylation step of glutamic residues of vitamin K-dependent precursor proteins of coagulation factors II, VII, IX, and X. Exposure to warfarin during organogenesis will result in a characteristic embryopathy, including nasal hypoplasia which may result in respiratory distress.
CNS abnormalities such as microcephaly, mental retardation, optic atrophy, and blindness have also been reported. Warfarin, therefore, is contraindicated in pregnancy.

Lovenox® (enoxaparin sodium) is a low molecular weight heparin administered subcutaneously which has anti-thrombotic effects, affecting coagulation factors Xa and IIa. Its indicated use is for prophylaxis of deep venous thrombosis which may lead to pulmonary embolism. It is contraindicated in patients with active bleeding. However, although not contraindicated in pregnancy, a special precaution is listed on the manufacturer’s product label for its use during pregnancy. There have been reports of congenital anomalies in infants born to women who received enoxaparin during pregnancy. There have even been reports of fetal death. Causality has not been determined. However, a warning has been issued by the manufacturer and a safety alert has been issued by the Food & Drug Administration on the use of enoxaparin with prosthetic heart valves in pregnancy, as of February, 2002. Alternative prophylaxis is with heparin during the entire pregnancy or heparin during the first 13 weeks, followed by warfarin until the middle of the third trimester, then heparin resumed while warfarin is discontinued. Heparin has low risk of complication or associated congenital anomalies when used during pregnancy. There is no general consensus about the end-point of heparin administration in pregnancy, nor whether an INR of >3.0 for aortic and >3.5 for mitral prostheses is adequate in a hypercoagulable pregnant patient.

Systolic blood pressure is minimally affected by pregnancy, with a maximum decline of 6% to 8% during early to mid-gestation and a return to pre-pregnant level at term. Because stroke volume is increased during pregnancy, the decline in systolic blood pressure is explained by increased aortic size and compliance. Maternal blood enters the placental intervillous space at a pressure of 70-80 mmHg and rapidly diminishes to approximately 10 mmHg as it passes into the densely packed, low resistance villi. It, therefore, suggests that systolic blood pressure should be maintained at least greater than 80 mmHg at all times. There is no evidence whether pulsatile flow is better for placental perfusion than non-pulsatile flow used commonly in cardiopulmonary bypass.

Maternal cardiac disease occurs in fewer than 2% of pregnancies. Rarely is elective or emergent cardiac surgery required. The fetal mortality rate during cardiopulmonary bypass exceeds 50% since optimal management of maternal interests may not coincide with fetal needs. The effect of cardiopulmonary bypass on the fetus or on uterine circulation has not been examined in a controlled study. Avoidance of hypothermia is recommended, if possible, because of the potential for producing fetal arrhythmias, including bradycardia. Because uterine blood flow is directly proportional to mean perfusion pressure, fetal bradycardia, frequently seen after initiation of cardiopulmonary bypass, may be related to decreased uterine perfusion pressure. It is recommended that high pump flows and high perfusion pressure be maintained to decrease incidence of fetal distress. It is not known whether loss of pulsatility, as occurs with cardiopulmonary bypass, has any effect on
placental blood flow.

All pregnant patients and most patients for emergency surgery require a rapid sequence induction to decrease the risk of aspiration. Etomidate is frequently used as a hypnotic induction agent when hemodynamic compromise is a high risk, since it preserves myocardial function, does not block sympathetics, and may support systemic vascular resistance. Although the fetal survival rate during cardiopulmonary bypass only approaches 50%, the survival rate for a preterm infant at 23 weeks gestation is only 1.8%. A C-section would not be tolerated nor indicated with acute mechanical valvular thrombosis.

Severe hemodynamic compromise is a well-known complication in acute mechanical prosthetic valve thrombosis, sometimes leading to left ventricular distention and failure, often resulting in death. The Trendelenberg position may cause further ventricular distention which may result in acute ventricular failure. Thrombolytics, specifically streptokinase, have been used successfully in a patient with aortic valve thrombosis at 6-7 weeks gestation. It is unknown whether the increased hypercoagulable state in mid and late pregnancy would have the same outcome.

Chest compressions are typically ineffective in pregnancy and are known to be inadequate in thrombosed aortic valves. Other than uterine displacement, cardiopulmonary bypass may be the only option to promote adequate placental blood flow.

Decreased systemic vascular resistance is commonly seen following cardiopulmonary bypass, especially in aortic valve surgery. Pregnancy causes a decreased SVR in later trimesters due to increased vascular size and compliance and the low resistance of the placental vasculature. Sensitivity to alpha-adrenergic agonists also declines during pregnancy. Uterine vessels in sheep are more sensitive to constriction from alpha-adrenergic agonists than are systemic vessels. Infusion of phenylephrine, epinephrine, and norepinephrine all decrease uterine blood flow in pregnant sheep and produce parallel decreases in myometrial and placental blood flow. Recently, studies have been published citing the use of ephedrine for prophylaxis against hypotension where regional anesthesia is chosen. Phenylephrine has been associated with improved umbilical cord gases at bolus doses up to 50 mcg. There are no human studies with norepinephrine in pregnancy, and it is indicated only if the risk to maternal survival outweighs the potential harm to the fetus.

Vasopressin has been used in pregnancy in low doses to treat diabetes insipidus without complication. However, since vasopressin is structurally similar to oxytocin, it is thought that the high doses required treat decreased vascular tone may induce pre-term labor. Although vasopressin causes splanchnic arterial vasoconstriction, it is unknown whether vasopressin causes uterine artery vasoconstriction. There are no clinical trials in animals or humans to date.
REFERENCES