PREGNANCY AND CARDIOPULMONARY BYPASS

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SUMMARY

The physiology of the female is substantially altered during pregnancy. Pregnant patients may also present with various kinds of cardiac diseases and the manifestations of these diseases may get worsened, and can be deleterious for both mother and fetus. Cardiac surgery with extra corporeal support during pregnancy has been associated with elevated fetal morbidity and mortality. Maternal morbidity and mortality seem more related to the subjacent cardiac disease and is not affected by cardiopulmonary bypass (CPB). Fetal mortality remains elevated as a consequence of CPB factors that stimulate uterine activity and contractions and reduce placental perfusion. Sub optimal gas exchange at the placental interface seems to be the main substrate for fetal bradycardia and distress. Monitoring uterine activity and fetal heart rate is of paramount importance in the prevention of fetal bradycardia. Adjusting the perfusion flow, perfusion pressure and FiO₂ can contribute to improve placental blood flow and allow for better exchange with fetal blood. Tocolytic agents may contribute to block uterine contractions and improve placental perfusion. This article reviews the influence of CPB factors on the mother, the influence of CPB on the fetoplacental unit and the principal aspects of CPB that can be associated with lower fetal and maternal morbidity and mortality.

Keywords : Pregnancy, Heart diseases, Cardiovascular surgery, Cardiopulmonary bypass, Open-heart surgery, Maternal outcome, Fetal-neonatal outcome.

Introduction

Cardiac surgery with extra corporeal support in a pregnant patient constitute a complex endeavor, as it represents the sum of anaesthetic, surgical and CPB effects on two individuals under biologically distinct situation. It is generally agreed that only emergency surgical procedures should be performed during pregnancy. Although maternal morbidity and mortality depends more on the pre existing cardiac disease and is not affected by CPB, fetal morbidity and mortality is high with extra corporeal support and cardiac surgery.

The concern of anaesthesiologist in such cases is that hormonal secretions from the corpus luteum and the placenta, as well as mechanical effects of the gravid uterus in a compromised cardiac status causes major physiological alterations in every organ system of the body. These effects can create serious problems to either of the two organisms.

There is a 1-4% incidence of cardiac disease in pregnancy as reported in united states¹,² and rheumatic heart disease accounts for 60% of the total.³ Although the incidence of cardiac disease in pregnant women varies in different countries, it is more prevalent in developing than in developed countries. Most specialists agree that the heart disease is the leading cause of death during pregnancy and delivery.⁴

Medical therapy is not always sufficient to drive a heart with a reduced functional reserve or acute complications in pregnant women. Despite maximal medical therapy, whenever the clinical condition of a pregnant woman with cardiac disease deteriorates, surgical correction is the only alternative to restore cardiovascular function and create conditions for the pregnancy to evolve normally.

Percutaneous balloon valvuloplasty may be promising in future when adequate imaging can be performed with safe or no radiation exposure, but presently it is prohibited in view of the radiation hazards associated with it to the fetus. Closed mitral valvotomy has been frequently performed with success to carry the mother through the pregnancy, with minimal or no complications.⁵,⁶

History

The earliest reports of cardiac surgery during pregnancy appeared in 1952, when Brock,⁷ Cooley and Chapman,⁸ Logan and Turner⁹ and Mason¹⁰ accomplished a total of eleven mitral commissurotomies with one maternal death and one premature delivery. In 1957 Daley et al⁴ performed a pulmonary commissurotomy and repaired an atrial septal defect at 6 weeks gestation, using extracorporeal circulation (ECC),
the patient survived the operation but had a spontaneous abortion three months later.

10 years later, Zitnick et al. summarized 20 cases of open-heart surgery during pregnancy and reported an overall maternal mortality of 5% and fetal mortality of 33%. In 1983, Becker reviewed 55 cases of open heart surgery done with ECC during pregnancy and found that although maternal mortality has decreased to 1.8%, fetal mortality had only slightly improved at 21.8%. Almost all the operations were performed during the second trimester of pregnancy where universal indication was progressive congestive heart failure unresponsive to medical treatment.

Born et al. has reported a single center study of 30 cases and documented a maternal mortality of 13% and a fetal mortality of 33% among patients with rheumatic valvular disease operated during pregnancy in the period 1981-1992. Weiss and co-workers reviewed the outcome of valvular disease operated during pregnancy in the period of 1984 and 1996. Surgery during pregnancy resulted in fetal-neonatal morbidity and mortality of 9% and 30% respectively. The maternal morbidity and mortality were 24% and 6% respectively.

Physiologic changes during pregnancy and their implications for CPB

It is of paramount importance to understand the physiologic changes that occur in mothers during pregnancy and the physiology of feto placental unit. From 12th to 36th weeks of pregnancy cardiac output gradually increases to a peak of 50% above resting levels. This rise in cardiac output is secondary to rise in intravascular volume. Oxygen consumption rises by 25% to 30% above non-pregnant levels. Rise in intra vascular volume along with oxygen consumption leads to a rise in cardiac preload causing an increase in stroke volume and heart rate, which finally leads to a high output state.

Mean red cell mass increases in pregnancy, but this is out weighed by an increase in blood volume, which leads to a fall in haematocrit level. Systemic and pulmonary vascular resistance decreases in pregnancy, which particularly affects the patients with right to left shunts. Thrombotic event increases during pregnancy because of a relative state of hypercoagulability. Uterine blood flow which is approximately 3% of total cardiac output increases by 15% during the third trimester.

All these changes are necessary to allow the mother to cope with the new and increased metabolic demands represented by fetoplacental unit.

Effects of Cardiopulmonary bypass

Adverse effects of CPB include changes in coagulation, alteration in the function of cellular and protein components of the blood, release of vasoactive substances from leukocytes, complement activation, particulate and air embolism, non pulsatile flow, hypothermia and hypotension. All these factors can compromise the delicate biological equilibrium between the fetus and the placenta. During prolonged operations such as valve replacement or repair of aneurysms, the deleterious effects of CPB act longer and their injury may be more pronounced.

Effect of Anaesthesia

The concern over the effects of anaesthetic agents on the fetal development and teratogenicity during cardiac surgery and CPB for pregnant patients exists whenever any drug is administered to a pregnant women, especially during the first trimester when fetal organogenesis occurs, but it appears that most anaesthetic agents, intravenous, inhalatory, and paralyzing agents are devoid of teratogenic effects and can be safely employed in a pregnant patient. Hypocarbia as a result of mechanical hyperventilation leads to a decrease in uterine blood flow by 25%. Although the blood pressure remains unchanged during hyperventilation, adverse effect on uterine blood flow was attributed to a decrease in venous return and cardiac output.

Cardiopulmonary bypass and fetal response

There are only few studies regarding the effects of maternal CPB on the fetus. Since the first report of the use of fetal heart recording during bypass by Koh and Co-workers in 1975, it has been known that fetal bradycardia occurs almost invariably at the onset of maternal CPB. What causes bradycardia at the beginning of the bypass is unknown, but it may be related to a decreased fetal oxygenation secondary to placental hypotension or to acid base changes. It has been postulated that starting a normothermic CPB with a high perfusion flow avoids the occurrence of fetal bradycardia.

Uterine contractions occurring on a background of a decreased perfusion and relative hypotension associated with CPB may produce inadequate placental perfusion with the resulting fetal response of bradycardia. A rate of 70 to 80 beats per minute represents a considerable degree of fetal distress. Elevating the perfusion flow and increasing the maternal PO₂ to 300 to 400 mmHg can correct it. Hence, Oxygen exchange at placental interface is favored by increasing both, the perfusion flow and arterial PO₂.

Both maternal and fetal catecholamines elevate due to stress, which increases the peripheral vascular resistance, which is not tolerated by the immature fetal myocardium. Anaesthetic agents produce maternal and fetal anaesthesia...
but fail to block the fetal response to the excess of circulatory catecholamines and other vasoactive agents.

Monitoring fetal heart rate and uterine activity can offer valuable information to the perfusionist regarding the placental blood flow and perfusion. At present, the best use of fetal heart rate monitoring is to allow adjustment of flow rates, should fetal bradycardia occur.

Fetoplacental unit response to cardiopulmonary bypass

Thirty to sixty minutes after the fetus is removed from the bypass a severe progressive respiratory acidosis develops. The underlying cause is probably activation of Eicosanoids products. The experiments have shown that inactivation of these products like prostaglandin E₂ and Thromboxane²², ²³ using indomethacin and corticosteroids can prevent this respiratory acidosis.

A more intractable metabolic acidosis develops six to eight hours after bypass is discontinued. This late metabolic acidosis is due to low cardiac output secondary to an increase in systemic vascular resistance because of an increase in catecholamine levels, and is a part of fetal stress response.

In the experimental setting of fetal CPB a spinal anaesthetic to the fetus has been shown to prevent this stress response and subsequent metabolic acidosis, but this is clearly impractical in the clinical setting of maternal CPB.

Although both indomethacin and steroids have been shown to be beneficial in the experimental settings, the detrimental effects of indomethacin on platelet function with subsequent risk of bleeding may place the mother at unreasonable risk, particularly in the perinatal period. Steroids would therefore be preferable in this context.

CPB effect on pregnant uterus

It has been suggested that the dilutional effect of bypass causes a decrease in hormonal levels; particularly progesterone, which produces, increased uterine excitability. Uterine contractions are particularly common during the rewarming phase after moderate or profound hypothermia and are considered to be the most important predictor of fetal death. They occur more frequently with increasing gestational age. Progesterone supplementation has been successfully used to stabilize the uterus around the time of the bypass. β₂ agonists have also been tried with good effects.

Uterine contractions in association with non pulsatile flow of CPB can produce insufficient irrigation of the placenta and determine the development of fetal hypoxia. Monitoring is therefore essential to allow early identification of contractions, so that they can be adequately treated before the development of fetal hypoxia and bradycardia.

Uterine and fetal monitoring during CPB

Monitoring uterine activity and fetal heart rate can offer valuable information regarding placental blood flow and perfusion, so it is a good recommendation to add these monitoring to CPB monitoring protocol of pregnant patients.

Cardiotocography

It is based on the surface detection of electrical activity, much like the conventional electrocardiography. An abdominal belt contains two sets of electrodes, one to monitor the uterine activity and the other to monitor the fetal heart beats.

Ultrasoundography and Doppler monitor

Doppler transducers are available to monitor fetal heart beats from the surface of maternal abdominal wall. These probes are difficult to maintain in place during the procedure. Smaller probes have also been used transvaginally to monitor fetal heart beats and umbilical cord flow, but they have not gained wide popularity.

Conduct of Cardiopulmonary Bypass

CPB effects on the fetoplacental unit can contribute to interrupt pregnancy and, to determine fetal death. During CPB the perfusionist’s attention should be directed at the placental blood flow, which can be optimized to offer the fetus the best conditions for oxygen exchange and, thus maintain its viability. In case of any indication of fetal distress, it should be treated aggressively. An obstetrician should be available in the operating room to monitor and adjust uterine and fetal parameters.

Positioning in the operating table

A 30 to 60 degrees pelvic tilt should be applied in the form of a wedge on the right side to avoid compression by the gravid and relaxed uterus over the inferior vena cava, particularly during the third trimester of pregnancy, to avoid hypotension after the induction of anaesthesia.

Anticoagulation

There is a small potential risk of placental haemorrhage, fetal abortion or premature labor with the use of heparin, although it does not cross the fetoplacental barrier. Recommendation for CPB on a pregnant patient is that ACT should be maintained between 480 to 600 seconds.

Priming

As a part of physiologic changes certain degree of anaemia always exist in pregnant patients. Plasma oncotic pressure is also 10 to 20% less than normal. Crystalloids,
haemodilution although successful, has been reported to cause fetal distress with low haematocrit. Perfusate volume should be minimum necessary to initiate bypass because of low oncotic pressure. A haematocrit of 25% obtain a better environment for the fetus, but the ideal haematocrit is 30 to 34%. Plasma albumin or colloids can favor tissue perfusion and contribute to avoid interstitial edema.

Diuretics should not be a part of routine protocol, but can be used to stimulate maternal diuresis if necessary. Furosemide is preferred to mannitol. Mannitol crosses the placental barrier and can stimulate fetal diuresis. An oncotically adjusted prime makes addition of mannitol or furosemide unnecessary and can avoid untoward effects of diuretics on the fetus. Before starting bypass, perfusate pH and temperature should be adjusted, to preserve fetal matenal exchanges.

**Pump flow**

Arterial flow should be 20 to 40% higher than flows used for routine CPB in non pregnant patients, to sustain adequate fetoplacental gas exchange during non pulsatile flow.

**Mean arterial pressure**

The best demonstration of an adequate arterial pressure is the fetal response to CPB, and the pump flow should be sufficient to maintain a mean arterial pressure above 70 mmHg (70 to 90 mmHg). During CPB on pregnant patients, high perfusion flow, high mean arterial pressure and a normal cardiotocography usually present a clear correlation.

**Gas flows**

To achieve a better perfusion and gas exchange of placental tissue and fetoplacental unit, CPB during pregnancy has to be conducted with a high FiO2 to produce an arterial PO2 of at least 200 mmHg. If fetal bradycardia occurs, PO2 should be elevated to about 400 mmHg along with other measures such as, increasing perfusion flow and pressure. High maternal arterial PO2 does not affect fetal organs and will not contribute to produce any ill effects.

**Hypothermia**

Gas exchange during hypothermia is reduced at the placental level. Hypothermia can increase uterine tone and contractions, and elevate uterine vascular resistance. Maternal bradycardia, ventricular arrhythmias and fibrillation are more common during hypothermia. Fetal mortality is higher when CPB is conducted with hypothermia. Significant hypothermia should be avoided unless extended aortic clamp time is anticipated or a circulatory arrest period is required. Rewarming produces uterine contractions and increases amniotic fluid pressure.

**Drugs**

Blood flow to the uterus is under a strong alpha-adrenergic control. Vasopressor with alpha adrenergic receptor effects can reduce uterine and placental blood flow. Whenever a peripheral vasodilatory effect is required during CPB an infusion of hydralazine can be administered without any untoward effects. Ephedrine and low dose dopamine does not appear to influence the uterine blood flow. Isoproteinrol has been recommended as the inotrope of choice soon after bypass, it has got a positive effect on maternal and fetal heart rate.

**Acid base management**

Significant changes in acid base balance are less likely to occur under normothermic CPB. The only changes seen are metabolic acidosis, as a consequence of reduced tissue perfusion and respiratory alkalosis because of excess gas flow in the oxygenator. Adjusting the perfusion and gas flows without the use of any drug can easily control both these changes.

During hypothermic CPB acid base disturbances can be more pronounced and there is no consensus regarding pH management during pregnancy. It is a good practice to manage pH according to alpha stat protocol. No recommendation has been found to add CO2 to the ventilating gas in order to keep a stable pH.

**Myocardial protection**

During long procedures and with the use of continuous cardioplegia, high potassium level in the maternal blood diffuses to fetal blood and originates fetal hyperkalemia. The hyperkalemia secondary to cardioplegia infusion affects the fetal myocardium and produces bradycardia, conduction disturbances or cardiac arrest. Regardless of the type of cardioplegia, the effluent should be aspirated from the right atrium or coronary ostia to avoid its mixing to the perfusate.

**Management of fetal bradycardia**

Fetal bradycardia indicates fetal distress, increasing pump flow and FiO2 are the usual measures taken to correct fetal bradycardia. If despite these measures fetal heart rate remains low, a small drip of ephedrine may be required. In few cases, it has been found that despite all management, fetal bradycardia persists for entire duration of CPB and reverts when normal circulation is resumed. When bradycardia prolongs to the postoperative period the risk of fetal death is substantially increased.

**Management of uterine contractions**

Most commonly, increased uterine contractions are associated with arterial hypotension, hypothermia, rewarming and dilution of pregnancy hormones such as progesterone.
Prolonged and intense contractions are associated with a higher incidence of fetal death. Beta agonist drugs can cease uterine contractions. Effective agents are terbutaline and ritodrine. Terbutaline can be given in the dose of 10 mg/min, which can be increased as necessary to 80 mg/min, and should be continued for four hours. Ritodrine is given at a dose of 50 to 150 mg/min and should be maintained for at least 12 hours.

**Conclusion**

A high risk of fetal morbidity and mortality is associated with CPB during pregnancy. Avoidance of sudden change in placental blood flow, maintenance of physiology of placenta to the normal as possible, managing the arterial oxygen tension along with the perfusion flow and pressure are the key determinants in the management of patient under CPB. Fetal bradycardia and increased uterine contractions need immediate attention and management. With the optimal care provided by the modern neonatal care units and considering caesarian section as an option, the deleterious effects of CPB can be avoided when the gestational age is above 28 weeks.

**References**