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Perioperative Fetal Monitoring during Acute Heart Valve Surgery in the 16th Week of Pregnancy: A Case Study with Follow up after Five Years

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Abstract

Cardiac surgery during pregnancy carries an extremely high fetal risk. When conducting anesthesia in the gravid patient care must be taken to avoid uterine contractions, and fetal hypoxia. Thus, in such cases, monitoring the fetal heart rate is of special importance, as early detection of fetal bradycardia can potentially prevent fetal harm.

We present a mother in the 16th week of pregnancy with endocarditis of the aortic valve associated with NYHA IV stage heart failure undergoing successful mechanical aortic valve implantation and reconstruction of the anterior leaflet of the mitral valve. The surgery was remarkable for an episode of serious maternal circulatory failure which was treated with several cycles of reperfusion and ephedrine. Perioperative fetal heart rate monitoring was carried out using Doppler ultra-sound technology. There was no critical fetal bradycardia encountered in the intra and perioperative period.

Birth was on term via vaginal delivery, with satisfactory weight and Apgar score. Dysmorphic face and multiple tarsal syndactylia were detected with accompanying partial dysgenesis of the corpus callosum on cranial ultrasound testing. These were attributed to an inherited gene mutation as a part of Pfeiffer syndrome, which, in fact, had familial aggregation on further investigation. Additionally, the newborn demonstrated symptoms of secondary hypadrenia possibly resulting from the serious maternal condition during the pregnancy, although the use of anesthetics in the 2nd trimester cannot be excluded as a cause.

During our follow up, both the somatic and mental development of the child remained unaffected. No cognitive or learning disabilities were apparent.

Keywords: Pregnancy; Infective endocarditis; Cardiac surgery; Fetal monitoring; Neurotoxicity; Anesthetic agents; Pfeiffer syndrome; Psychosomatic functions; Secondary hypadrenia

Introduction

The most frequent cause of maternal mortality during pregnancy is heart disease with a 1-3% occurrence [1]. Infective endocarditis is particularly rare during pregnancy with an incidence of around 0.006% according to previous investigators. However, in cases of infective endocarditis, both maternal and fetal mortality rates remain high; 19-33% and 15-29%, respectively [2]. Cardiac surgery for endocarditis should be avoided during pregnancy, if possible, but the cases, in which maternal mortality is potentially reducible and the mortality of the procedure is not significantly higher than that of the non-pregnant, should be considered for surgery with the following indications: 1) severe cardiac failure; 2) presence of a vegetation that is prone to embolic dissemination; 3) uncontrollable infection.

Fetal mortality associated with cardiac surgery with cardiopulmonary bypass has been as high as 18.6% in the past 20 years [3]. Besides heart failure, factors such as emergent operation, re-operation, long aortic cross clamp time [4], hypothermia [5] and advanced maternal age (>35 years) also increase operative risk to the fetus. However, high fetal mortality resulting from cardiac surgery is reduced when fetal monitoring of the heart rate is applied [6,7]. Early detection of bradycardia allows for early intervention in order to prevent permanent damage to the fetus. As a result of anticoagulation, only non-invasive monitoring is to be used, such as fetal ultrasound, phonocardiography or abdominal EKG. Using a tocodynomometer is also advised after the 18th week of pregnancy [8], because spontaneous contractions of the uterus during the procedure can compromise uterine perfusion by reducing venous return [6].

Fetal malformations are among the most feared complications of non-obstetric operations. Although serious maternal disease itself can cause malformations [9], anesthetic use is also well-known for its potential to interfere with DNA synthesis and mitosis which may result in teratogenicity. Tests on animals have shown that general anesthetics used in the 2nd trimester of pregnancy have a negative impact on neurogenesis, which have been proved to have a detrimental impact on memory, resulting in learning disabilities [10]. However, at the present time, there is limited data on the human teratogenicity of anesthetics [7]. Most human studies that deal with the fetal effects of anesthetics and/or surgical procedures focus on the outcome measures at birth only; long-term data on cognitive and learning development in human subjects is lacking.

In our case study, we present the operation of a woman with aortic valve endocarditis associated with severe heart failure in her 16th week of pregnancy, allocating special focus on the importance of perioperative fetal monitoring. Subsequently, we discuss the anesthesiologic considerations of this case regarding the physiologic changes of pregnancy, the maintenance the uteroplacentary perfusion, and the teratogenicity of anesthetics. Follow-up results of the child's cognitive development at age 5 are also presented.

Case Report

A 24-year-old woman with no previous history of cardiac disease was at the beginning of the second trimester of her second pregnancy when she experienced two weeks of having fever after a dental procedure. Despite receiving 18 days of antibiotic treatment for UTI, she remained subfebrile and subsequently developed shortness of breath accompanied by gout and a heart murmur. Cardiac investigation found severe aortic insufficiency with ultrasonographic evidence of a mobile vegetation and an opened paravalvular abscess. The patient was admitted in NYHA IV status, with resting tachypnea and orthopnea.

On arrival, she presented with 131/min sinus tachycardia, a BP of 120/58 Hgmm an O_2 saturation of 97% and a pCO_2 of 28.1 Hgmm, with the administration of 2 l/min of nasal O_2 in a semi-sitting position. The skin temperature was 37.3 degrees Celsius. CBC showed anemia with an elevated ESR and leukocytosis (Hgb: 103 g/l, ESR: 55 mm, WBC: 13.7 neutr. %: 85,2). Her metabolic panel was normal. We administered Ampicillin in a 2 g/4 hour dose.

The patient underwent transesophageal echocardiography (TEE), which found a volume loaded left ventricle and a tricuspid aortic valve with a 14 mm mobile vegetation of the left coronary cusp and an erosion of the non-coronary cusp, which resulted in grade IV insufficiency. Examination of the septum showed an opened perivalvular abscess. Fetal ultra-sound examination, which estimated the pregnancy to be 15 weeks and 5 days, showed no fetal abnormalities.

Due to the high fetal risk of the operation, perioperative fetal monitoring was carried out with the adult transducer of our Vivid I (GE) ultra-sound. (Figures 1,2). Monitoring of the fetus was aided by an obstetrician in the operating room. In the mother basic monitoring was implemented in order to avoid the risk of colonization and placentary embolization with the use of Schwann-Ganz catheters and PiCC lines.

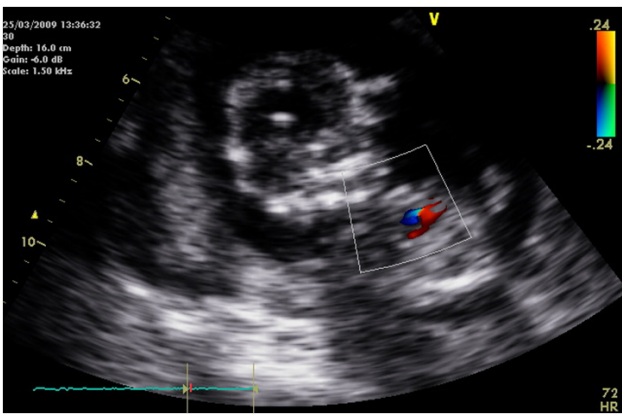

Figure 1: Ultra-sound image of the foetus, colour Doppler

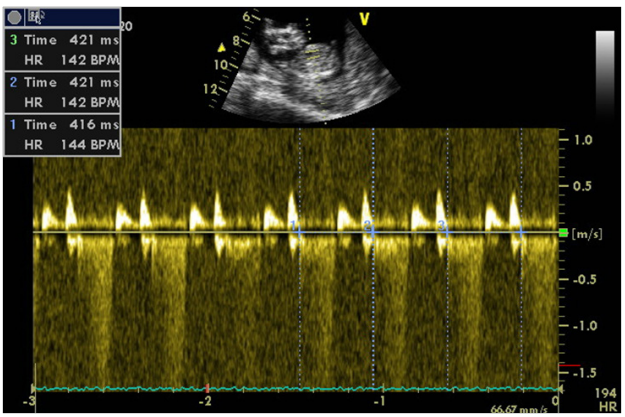

Figure 2: Determining fetal heart rate using pulsatile Doppler [positive wave: mitral inflow (E/A wave), negative wave: aortic outflow]

During preparation, 7.5 mg midazolam and 40 mg pantoprasol were administered. The heart rate was 125/min and BP: 110/45 Hgmm. Induction was not possible in a supine position due to dyspnea, therefore we performed rapid induction in a semi-sitting anti-Trendelemburg position using 5 mg midazolam, propofol TCI 2 mikrogr/ml, 10 mikrogr sufentanil and 4 mg bolus pipecuronium. During intubation, a Sellic manoeuvre was applied.

Following induction, circulatory instability did not occur. In order to maintain the lowest possible doses of anesthetics in the shortest possible exposition, we combined several different substances: Up until the initiation of cardiopulmonary bypass (CPB), propofol (TCI 1.5-2.0 mikro/ml) and isofluran (0.5-1.0%, FiO_2 1.0-0.7) were used; after starting extracorporeal circulation, propofol was stopped, and sevofluran (1.5-2.0% FiO_2 0.7) was used for the rest of the operation. Additionally, sufentanil (TCI 0.25-0.30 ng/ml) was used for the entire duration of the operation. To avoid compression of the superior vena cava, the operating table was tilted 15 degrees to the left. Reduction of the uterine tone was achieved by administering a slow infusion of 240 mg aminophyllin and 2x1 gram $MgSO_4$ at the beginning of the operation, and another 1 gram bolus of $MgSO_4$ was given upon releasing the aortic cross clamp.

Prior to starting CPB, 20000 I.U,+ 10000 I.U of Heparin Sodium was given to maintain a 400 s of ACT during the pump run (403-508 s). One unit of selected red blood cells was given to the pump prime, which was repeated after starting CPB. During CPB, pulsatile flow was used with 3 l/m^2/min cardiac output and a mean arterial pressure above 65 Hgmm. During surgery, Hct was between 0.27-0.33. In order to maintain an adequate perfusion pressure, 5 mg boluses of ephedrine were given in a total of 15 mg before CPB, and an additional 55 mg during CPB. Two attempts to wean from CPB were unsuccessful despite repeated doses of ephedrine, therefore another cycle of reperfusion was initiated while ephedrine was set in continuous infusion. The dose of ephedrine during those weaning attempts and thereafter was a total of 25 mg. The continuous infusion was set at 25-12 mg/hour. 200 mg of protamine sulphate was given to counteract the heparin effect. During the operation, a 21 mm mechanical valve (St Jude) was implanted and a pin-size fenestration on the anterior leaflet of the mitral valve was closed. Total CPB time was 110 minutes, aortic cross clamp time was 68 minutes and the total time of anesthesia was 290 minutes. For the whole duration of surgery we tried to avoid hypocapnia (pCO_2 42.1-45.6 Hgmm) and maintain normothermia (35.6-36.7 Celsius). We did not encounter critical fetal bradycardia; fetal heart rate during the operation was 141-185/min.

The patient's circulation demanded continuous ephedrine support in the first two hours. Following termination of ephedrine, metoprolol was started due to sinus tachycardia. After 9.5 hours of respirator support, the patient was extubated. Postoperative bleeding was 300 ml. Due to anemia, another 2 units of red blood cells were transfused. Sonographic fetal monitoring was continued in the immediate postoperative period and subsequently in the surgical intensive care unit (SICU).

TEE on the 1st postoperative day showed diffuse hypokinesis and reduced global left ventricular function with an EF of 35%. Digoxin therapy was induced and a therapeutic dose of enoxaparin was started and maintained until birth. The patient was transferred from the SICU to our general telemetry unit on the 4th postoperative day and the rest of her postoperative course was uneventful. Cardiac function gradually increased, EF was 60% on day five. Microbiological testing of the aortic valve showed alpha haemolytic Streptococcus, therefore an additional 6 weeks of penamecillin was administered.

In the 40th week of pregnancy, the patient was diagnosed with hypothyroidism (TSH: 0.0045mE/l, FT3:10.42 pmol/l) and a thyroid cyst was found with subsequent propylthiouracyl therapy starting.

In the same week, a baby girl was delivered via normal vaginal delivery with a weight of 3200 grams and a height of 48 cm. The 1- and 5-minute Apgar scores were 8 and 9, respectively. At birth asymptomatic hypoglycaemia was detected along with a dysmorphic face, a flat nasal bridge, micrognathia, low set ears, plagiocephaly, broad hallux and polysyndactilia on the feet with toes arranged III-IV on the left and II-III-IV on the right foot. Cardiac ultrasound found an ostium secundum type ASD with a small left to right shunt. Cranial ultrasound imaging showed a midline shift and partial dysgenesis of the corpus callosum. Endocrinology testing found central hypadrenia, for which substitutional hydrocortison therapy was initiated. Genetic testing found a mutation of gene FGR1, which – in the presence of the corresponding clinical findings – was interpreted as a mild form of type-1 Pfeiffer syndrome. Family history revealed that the father, the father's sibling and the maternal grandmother had dysmorphic signs of Pfeiffer syndrome, and that the grandmother had undergone open ASD closure at the age of six.

Surgical procedures of the infant included a reconstructive skull surgery at 6 months, a correction of syndactilia at 12 months, and an inguinal hernioplasty at three and a half years of age.

Follow-up of the child's c cognitive development was carried out at the age five and a half years by Snijders-Oomen nonverbal testing, which showed an IQ of 112 consistent with a developmental level of six years of age. Her psychological function, broad intellectual skills and cognitive functions (such as motor function, alertness, concentration, learning, memory and speech) were all satisfactory for her age. Adaptive behavior (separateness, relationships and pliancy) tests resulted in similar findings.

Discussion

Importance of Perioperative Fetal Monitoring

The fetal risk resulting from the abovementioned procedure was extremely high due to the advanced stage of the maternal disease (NYHA IV) and the urgent nature of the surgery. According to previous investigations, cardiac surgery carried out in NYHA IV stage carries a fetal risk of 66% [4]. Regarding the indication and the timing of surgery, it is important to consider the interests of both the mother and baby. Since the mother and fetus should be treated together, fetal monitoring is imperative. When cardiac surgery is to be performed after the 26th week, caesarean section can be carried out as an alternative option prior to the operation in order to avoid fetal complications. However, in such decisions, one must also consider the risks of premature birth.

Placental hypoperfusion commonly occurs during cardiopulmonary bypass (CPB). Bradycardia occurring within the normal range of fetal heart rate (120-160/min) indicates hypoperfusion or hypothermia, but respiratory acidosis of the mother as well as anesthetic use can also lower the heart rate. Serious fetal bradycardia (70-80/min) is an indication of asphyxia. Early detection of conditions which endanger the fetus provides us with a chance for carrying out necessary interventions, such as increasing the oxygen transfer capacity of the mother, increasing perfusion pressure, decreasing tonicity of the uterus, treating any acid base imbalances and correcting hypoglycaemia. During fetal monitoring one has to be aware of the fact that fetal heart rate variability is not a reliable indicator of fetal well-being during anesthesia, as opiates penetrating the placenta interfere with its accurate assessment [7].

Perioperative fetal monitoring after week 16 reduces the risk of placental hypoperfusion and fetal mortality [6-8]. However, out of the 150 documented cases of pregnant women undergoing cardiac surgery with ECC in the literature between 1991 and 2013, fetal monitoring was used in only 29 [3]. Our case presents an example of successful intraoperative fetal monitoring in the 16th week of pregnancy.

Anesthesia of the Gravida

Physiological changes during pregnancy have paramount importance in terms of anesthesia. Increased oxygen consumption and decreased functional residual capacity together cause early desaturation of the mother even after a very brief period of apnea. From the second trimester onwards edema of the oropharyngeal tissues leads to difficulties regarding intubation. The Mallapanti score is a very good indicator for this [6]. As tonicity of the lower esophageal sphincter is reduced and the stomach is compressed, especially beyond the 20th week of pregnancy, a pregnant woman is the equivalent of a patient admitted with a full stomach. Therefore, rapid induction of anesthesia is necessary in such cases.

During pregnancy, sensitivity to anesthetics is increased [11], therefore we used reduced doses of inhalative narcotics and propofol. By combining anesthetics (at first propofol in TCI pump and isofluran, followed by only isofluran and finally sevofluran), we managed to reduce the dose of each individual narcotic. In contrast, certain authors, basing their conclusions on the results of animal tests, suggest that multi-targeted anesthesia is a risk factor for neurodegeneration [12] of the fetus.

Experience from several case reports provides the basic guidelines of extracorporeal perfusion in pregnant women. Principles regarding anesthesia and extracorporeal perfusion are summarized in Table 1.

Principle	Comment
Uterine tonicity should be monitored	
Ensure high Sat O^2	Maintain Haematocrit > 0.28 (8)
Normocapnia, moderate hypercapnia	Hypocapnia reduces uterine blood flow. Major hypercapnia leads to fetal acidosis
Avoid hypoglycaemia	Add hypertonic glucose solution as a filling liquid to the CPB
Use of tocolitics ($MgSO_4$, ritodrine, terbutalin)	
Alpha-Stat pH management	
Ensure core temperature of 32 – 34°C	Lack of fetal thermoregulation. Hypothermia increase fetal mortality (5)
Ensure satisfactory venous return from IVC	IVC cannulation
Avoid aortocaval compression	A 15 degree left tilt of the operating table.
Pulsatile CPB flow suggested	Improved placental flow in animal tests
Pump flow > 2.5 l/min/m^2 (30-50% above calculated cardiac output)	The cardiac output during pregnancy is higher
Mean perfusion pressure > 70 Hgmm.	Uterus perfusion depends on the mean systolic pressure
Ensure short pump time	

Table 1: Principles of anesthesia and extracorporeal perfusion during cardiac surgery of pregnant women

Uteroplacentary Perfusion

Perfusion of the uterus is not autoregulated, therefore blood flow is determined by the mean arterial pressure, the perfusion pressure of the intervillous space, and the resistance of the spiral arteries. Perfusion of the placenta is reduced in the settings of low mean arterial pressure, low cardiac output, and an elevated venous pressure (aortocaval compression, unsatisfactory cannulation of the inferior vena cava). ECC poses an increased risk for the fetus for a number of reasons: the non-pulsatile flow, thinappropriate perfusion pressure, low pump flow, uteroplacentary embolisation and the release of renin/catecholamine can amount to serious complications [4,7,8]. There is no solid data regarding fetal effects of cardiac surgery with ECC.

Intravenous anesthetics do not significantly influence perfusion of the uterus, while inhalative anesthetics in low to medium doses improve circulation, as they cause vasodilation in uterine arteries and reduce the tonicity of the uterus. According to data based on animal tests, high concentrations (1.5-2 MAC) of isofluran or desfluran cause haemodynamic instability, thereby corrupting placental blood flow [11]. We did not use high concentrations of gas narcotics.

The effects of vasoconstrictors and positive inotropic agents on the uterus are not fully understood and any recommendations are based on animal tests. Alpha adrenergic stimulation increases vascular resistance of the uterus which is somewhat compensated by their effect of increasing the mean perfusion pressure. With this in mind, it is understandable that ephedrine and phenilephrine are the agents suggested for circulatory failure when the uteroplacentary perfusion is to be maintained. These two agents also improve the fetal acid base balance in caesarian sections carried out in spinal anesthesia [13]. There is no current data for the safe use of Levosimendan. Animal tests regarding Dopamin are inconclusive [8]. Noradrenaline and adrenalin both decrease uterine perfusion and are therefore not recommended [14]. In our case, after weaning from ECC, serious circulatory failure occurred. In order to avoid the use of catecholamins, we applied multiple cycles of prolonged reperfusion and a high dose of ephedrine. We did not register any sign of fetal hypoxia.

Teratogenicity

Several authors consider the second trimester as the most ideal time for maternal or intrauterine fetal operations [4]. The main reason for this is that the first trimester is the most vulnerable time for teratogenic occurrences and the third trimester carries the highest risk for the mother. Animal tests provide evidence that anesthetics used in the earlier developmental stages of the brain provoke neurodegeneration, which lead to learning disabilities [15]. However, in the development of the human nervous system, the second trimester of pregnancy seems to be the most vulnerable period as this is the stage of neurogenesis and migration [10]. In the fetus, GABA and glutamate carry a trophic role in the development of the nervous system. GABA and anesthetics that work on NMDA receptors were shown to have an effect on both neuroapoptosis [16] and synaptogenesis, and also influenced the plasticity of the developing nervous system [17,18]. Furthermore, the use of nitrous oxide is not recommended as it was proven to be teratogenic in animal tests [19]. Ketamin, also used in animal tests, has a fetal neurodegenerative effect and it increases neuroapoptosis and the tone of the uterus [20].

It is known that apart from anesthesia, serious maternal illness or a surgical intervention can also interfere with the development of the nervous system [21]; however, large cohort studies failed to determine the extent of which these factors affect the development of learning disabilities. We did not find any follow up data regarding cognitive function following fetal exposure to anesthetics.

In our case, dysmorphia and syndactilia registered at birth were a part of an inherited gene mutation called Pfeiffer syndrome, aggregating in family members. Partial dysgenesis of the corpus callosum and hypopituitarism, however, are not part of this syndrome. The operation was carried out in the second trimester, which coincides with the formation of the hypothalamus-hypophysis-adrenal gland axis and the activation of its endocrine function [22]. Therefore, it is reasonable to suggest that the central hypadraenia registered at birth was caused by either the mother's serious condition or the anesthetics used for her surgery. However, we did not find pertinent literature to further support either hypothesis. Currently, at age 5, the child's cognitive functions and adaptive behavior pertain to that of the appropriate age group; learning disabilities that suggest disturbance of synaptogenesis, are not apparent.

Conclusion

Our case study presents an example of successful perioperative fetal monitoring during cardiac surgery with CPB in the second trimester of pregnancy. The mother's circulatory failure during the procedure was successfully managed with high doses of ephedrine. During our follow up at age five of the child, no cognitive or learning disabilities were apparent. This report with its long-term follow-up of cognitive functions could provide valuable data for future surgical interventions involving human fetuses.

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