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Case Report

Anesthesia for Percutaneous Fetal Pulmonary Valvuloplasty: A Single Center Experience in Five Cases

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ABSTRACT

Despite treatments for congenital heart diseases(CHD) have made impressive progress, some CHDs still have a poor prognosis even with early-stage surgeries. Ever since the first procedure reported in 1991, fetal cardiac intervention (FCI) has improved the outcomes for patients with pulmonary atresia with intact ventricular septum. However, few cases have been reported in China. The aim of this study is to retrospect the 5 cases in our medical center to summarize the key points of anesthesia management for FCI.

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Prevalence of congenital heart diseases has been increasing during recent decades due to the progress of prenatal diagnostic techniques. The incidence of CHD in the United States is reported as 0.4%-1%, 0.69% in Europe, and 0.93% in Asia (1). Even though significant progress has been made in neonatal surgical and interventional treatments, patients with pulmonary atresia or critical pulmonary stenosis with intact ventricular septum sometimes have to receive palliative treatments even with prenatal diagnosis and early postnatal treatment, and their long-term survival rate and life quality could be seriously influenced with palliative univentricular circulation. Besides, some of them may develop non-immune hydrops, heart failure and even fetal demise without prenatal treatment (2).

Ever since the first fetal cardiac intervention (FCI) for fetal aortic valvuloplasty was reported by Maxwell et al. in 1991, the procedure has been performed by medical centers in various parts of the world (3). The indications have expanded to pulmonary atresia or critical pulmonary stenosis with intact ventricular septum (PA/IVS or CPS/IVS), and hypoplastic left heart syndrome (HLHS) with intact or restricted atrial septum (4-8). FCI (median gestation week at intervention: 26 + 4 weeks) has an earlier window compared to EX utero Intrapartum Treatment (EXIT procedure) (9, 10), and it is much less invasive than fetal open surgery.

Few cases of FCI have been reported in China. Reported cases of fetal pulmonary valvuloplasty are fewer than aortic valvuloplasty due to

the criteria of candidates. Fetuses with right ventricle-dependent coronary circulation are contradicted to FCI because the relief of right ventricle pressure would significantly diminish coronary circulation. In this article, we retrospect the 5 cases of fetal pulmonary valvuloplasty in our medical center, in order to summarize the key points of anesthesia management for FCI.

Case Presentation

The 5 patients underwent 7 FCIs in our medical center from September 2016 to April 2018. Maternal and fetal basic information is shown in the Table. All mothers were evaluated as ASA I or II. The mother in case 3 had "pulmonary valve injunction incision" at the age of 3 because of "pulmonary stenosis", and she had "percutaneous pulmonary valve replacement" due to pulmonary regurgitation later. She had suffered from lower extremity edema during pregnancy, but it alleviated after treatment. Her preoperative transthoracic echocardiogram showed medium pulmonary regurgitation (within prosthetic), and she was graded as NYHA II. All fetuses were diagnosed as pulmonary atresia or critical pulmonary stenosis with intact ventricular septum, hypoplastic right ventricle and tricuspid regurgitation by prenatal cardiac ultrasound. All cases were ruled out right ventricle-dependent coronary circulation.

Preoperative preparation: The Departments of Obstetrics and Gynecology, Pediatrics, Pediatric Surgery, Neonatal Intensive Care Unit, and Anesthesiology at Guangdong Cardiovascular Institute & Guangdong General Hospital, Guangzhou, China, had multidisciplinary rounds to confirm indications and gained patients' consents for the procedure (Figure). After routine preoperative preparation and ultrasound confirmation of a proper fetal position, patients entered the operation room. Venous lines and invasive arterial blood pressure were accessed.

Anesthesia induction and maintenance: Induction started right after the re-confirmation of a suitable fetal position by ultrasound. After rapid induction of midazolam 0.03 mg/kg, fentanyl 3 μg/kg (or sufentanyl 0.3 μg/kg), rocuronium 0.6-0.8 mg/kg, an endotracheal tube was inserted. Continuous inhalation of desflurane or sevoflurane with minimal alveolar concentration (MAC) 1-2, and venous infusion of propofol 2-4 mg/kg/h, and remifentanyl 0.1-0.2 μg/kg/min was used to maintain the Narcotrend Index between E1-F0. Phenylephrine and/or dopamine was used to maintain maternal invasive blood pressure between 90-120/50-70 mm Hg.

The procedure was performed under the guidance of trans-abdominal ultrasound. The transplacental path was chosen. An 18G gauge followed by a guidewire and a balloon was inserted into the fetal pulmonary artery through the fetal right ventricle and pulmonary valve. Fetal heart rate(FHR) decreased obviously when the guidewire or balloon was within the fetal heart. It recovered after fetal intracardiac injection of epinephrine 1 μg/kg and/or atropine 0.1 mg/dose.

Maternal venous injection of epinephrine (100-200 μg/dose, followed by urapidil 25-50 mg/dose) was used when the fetal intracardiac injection was difficult to access. FHR regained afterward. In case 1 and 3, the fetuses suffered from cardiac tamponade and fetal hemodynamic instability lasted for 3-5 minutes. Maternal venous injection of epinephrine and an emergency fetal pericardiocentesis was performed. FHR recovered afterward. Considering the risks to continue the procedure, the interventions stopped and restarted the next day. Anesthesia management was similar in the second attempts, but sevoflurane was decreased to MAC 1-1.5, to maintain the Narcotrend Index between D2-E1. All 5 patients received successful interventions eventually.

All mothers returned to the Surgical Intensive Care Unit (SICU) for observation after the procedure. Endotracheal tubes were removed on the same day, and the patients were transferred back to the ward, where they received fetal monitoring for a week before discharge. All mothers survived without major complications (aspiration, damage to the teeth, damage to the larynx, cardiovascular complications, pulmonary edema, brain damage due to asphyxia). All fetuses survived till delivery and were sent to the Neonatal Intensive Care Unit (NICU) for further treatments. The newborn in case 1 received modified Blalock-Taussig Shunt and pulmonary valve commissurotomy on day 8. He was discharged a month later, and still on follow-up. Newborns in

Table. Basic Characteristics of the Five Cases.

Characteristic	Case No. 1	Case No. 2	Case No. 3	Case No. 4	Case No. 5
Maternal Age (yr)	39	37	33	27	30
Gestational week at FCI	28	28	30	30	28
Delivery Gestational Week	38	35	38	38	37
Mode of Delivery	CS[a]	SD[b]	CS	CS	SD
Infant Weight at Delivery (g)	2970	3390	3060	3010	2650
Apgar Score (1 min/10 min)	10/10	9/9	10/10	5/8	10/10
Post Natal Treatment	Modified B-T shunt and pulmonary valvuloplasty on day 8	PBPV[c] on day 19	PBPV on day 9	Closed pulmonary valvuloplasty at 1 month. Died for MODS[d] a week later	PBPV on day 13

[a]CS, cesarean section; [b]SD, spontaneous delivery; [c]PBPV, percutaneous balloon pulmonary valvuloplasty; [d]MODS, multiple organ dysfunction syndrome.

case 2, 3 and 5 received percutaneous balloon pulmonary valvuloplasty and obtained biventricular circulation. The infant in case 4 suffered from intrauterine infections and stayed in NICU for 6 weeks before receiving closed pulmonary valvuloplasty. He died of multiple organ dysfunction syndrome a week later.

Discussion

With significant progress of the techniques, there have been procedures facing the fetus as a patient. Prenatal interventions or surgeries may improve fetal survival rate, postnatal prognosis and life quality for some congenital diseases. Potential candidates for FCI include fetuses with critical aortic stenosis evolving with HLHS, PA/IVS or CPS/IVS, intact or restricted atrial septum with HLHS. Indications for fetal pulmonary valvuloplasty include PA/IVS and CPS/IVS, with a hypoplastic right ventricle and triscupid valve annulus z score of < 2. Contradictions include right ventricle-dependent coronary circulation. Unlike the fetuses who might benefit from such procedures, mothers often face the risks of the procedure and anesthesia, but received few benefits. Therefore, a comprehensive consent should be obtained and maternal safety should always be the priority. Perioperative management for such procedures is similar to that for non-obstetrics procedures during pregnancy, which includes concern of maternal safety, avoidance of teratogenic drugs and fetal hypoxia, and prevention of preterm delivery (11).

Maternal Changes during Pregnancy

There are profound changes in various systems during pregnancy. Cardiac output starts increasing at early gestations and plateaus at 28-32 weeks. The increase of plasma volume and blood flow to the placenta also contributes to the cardiac output. Increased oxygen need and consumption leads to an increase in tidal volume during pregnancy. With the enlargement of the uterus and elevation of the diaphragm, and the tense of esophageal sphincter decreases, the risk of reflux and aspiration during pregnancy is higher. At the same time, Mallampati class is prone to fall to class 3 or 4 due to pharyngeal tissue edema. Therefore, the difficult upper airway should be a concern during maternal anesthesia. Generally speaking, pregnant patients' are more sensitive to anesthetics. For instance, MAC of inhalation anesthetics decreases, and spinal anesthetic plane expands. Besides, pregnancy may lead to sensitiveness to non-depolarizing muscle relaxants (12-14).

Fetal Physiology

Fetal systems are immature and vulnerable, and fetal physiology could be very different even from newborns. Since the placenta is the only source the fetus has access to nutrition and oxygen. Anesthetic management should avoid maternal hypo-

Figure. The Multidisciplinary Team.

tension or asphyxia, as well as drugs reducing blood flow through the placenta. It is still controversial whether the fetuses can feel pain, or when they start to feel. However, there is evidence to support that fetuses may physically respond to noxious stimuli and stress, regardless they are conscious or not(15). Therefore fetal anesthesia should not be ignored during fetal procedures even they are minimally invasive.

Preoperative Evaluation and Anesthesia Management

Maternal preoperative evaluation should focus on cardiopulmonary function and airway evaluation. A spinal examination is necessary for patients who are planned for spinal or regional anesthesia. Laboratory examinations should include blood routine tests, coagulation, fetal blood type, etc. Fetal examinations should include estimation of fetal weight, volume of amniotic fluid, and the placental position.

Fetal procedures can be performed under local, regional, or general anesthesia. Maternal analgesia can be satisfactory under local anesthesia. For some complicated procedures, regional or spinal anesthesia can prepare for an emergency cesarean section. Fetal analgesia can be achieved by injecting a cocktail of fentanyl, rocuronium, and atropine (to prevent decreasing heart rate) through the umbilical vein or fetal intracardiac injection, or maternal venous infusion of remifentanyl (16). The advantages of general anesthesia (GA) for FCI include: 1. GA provides satisfactory analgesia for both the mother and the fetus, as well as inhibition of uterine contractions, to prevent fetal movement and preterm labor; 2. it conveniences intraoperative maternal fluid management and hemodynamic management; 3. inhalation anesthetics and opioids in maternal systems can pass through the placenta, reduce fetal response to noxious stimuli and immobilize the fetus, thus reduce or avoid fetal injection of opioids and muscle relaxants. However, the previous report shows no significant difference in outcomes among different anesthetic methods (10).

Take Home Message
Fetal cardiac intervention (FCI) can be an effective treatment for some congenital heart diseases such as pulmonary atresia or critical pulmonary stenosis with intact ventricular septum. For some patients evolving with hypoplastic right ventricle syndrome, FCI could be an option to obtain biventricular circulation and better outcomes.
Anesthesia management is similar to that of non-obstetric procedures during pregnancy, which should take both maternal and fetal physiological conditions into consideration. General anesthesia can provide enough maternal and fetal analgesia, as well as satisfactory fetal immobilization and uterine relaxation.
Fetal hemodynamic instability is a common and dangerous complication during FCI. Apart from fetal muscular/intracardiac injection, maternal venous injection of epinephrine could be an effective way to resuscitate fetal hemodynamic instability (FHI).

Uterine relaxation is usually maintained by a high concentration of inhalation anesthetics (MAC 1.5-2) during GA, and venous infusion of nitroglycerin can enhance the effect. However, tocolysis is usually associated with maternal hypotension and placental hypoperfusion, as well as fetal myocardial depression. Maternal vasopressors are often necessary during fetal procedures. There is evidence that supports supplemental intravenous anesthesia with lower doses of inhalation anesthetics can provide enough uterine relaxation, as well as better maternal-fetal hemodynamic stability (17, 18).

Complications and Treatment

Maternal anesthesia-associated complications include reflux and aspiration, teeth damage, larynx damage, pulmonary edema, awareness and brain damage due to asphyxia. Other complications include intrauterine fetal death, premature rupture of membranes, and preterm labor (10).

Fetal complications of FCI include pericardial effusion, arrhythmia, and growth cease. The most common is fetal hemodynamic instability (FHI). According to previous reports, the incidence rate can be as high as 45%. The definition of FHI is fetal heart rate ⩽ 110 beats per minute, and lasting for over 30 seconds, with concomitant dysfunction of the dominant ventricle (19). It can be multifactor induced, including inhaling anesthesia, pericardial effusion, hypoxia, acidosis, parasympathetic stimulation or sympathetic inhibition due to myocardial traction during the procedure (20-23). Fetal muscular and/or intracardiac administration of epinephrine is considered to be the most effective method of FHI resuscitation (24). In the 5 cases in our center, we successfully resuscitated FHI by maternal injection of epinephrine. It could be an effective method for fetal resuscitation especially when the fetal intracardiac/muscular injection is difficult to access. However, it should not become a routine treatment because of the significant influence to maternal hemodynamics. It should only be used under emergency, and maternal blood pressure should be carefully controlled in case of cardiovascular complications. Meanwhile, its efficacy and safety are yet to be confirmed by further researches due to the inadequate case number.

The authors declare no conflicts of interest.

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