Review Article

Foetal surgery: Anaesthetic implications and strategic management

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ABSTRACT

Intrauterine surgery is being performed with increasing frequency. Correction of foetal anomalies *in utero* can result in normal growth of foetus and a healthier baby at delivery. Intrauterine surgery can also improve the survival of babies who would have otherwise died at delivery, or in the neonatal period. There are three commonly used approaches to correct foetal anomalies: open surgery, where the foetus is exposed through hysterotomy; percutaneous approach, where needle or foetoscope is inserted through the abdominal wall and the uterine wall; finally, *ex utero* intrapartum treatment (EXIT) surgery, where the intervention is performed on the baby before terminating the maternal umbilical support to the baby. Anaesthetic management of the mother and the foetus requires good understanding of maternal physiology, foetal physiology, and pharmacological and surgical implications to the foetus. Uterine relaxation is a critical requisite for open foetal procedures and EXIT procedures. General anaesthesia and/or regional anaesthesia can be used successfully depending on the nature of foetal intervention. Foetal surgery poses complications not only to the foetus but also to the mother. Therefore, the decision for undertaking foetal surgery should always consider the risk to the mother versus benefit to the foetus.

Key words: Anaesthesia for foetal surgery, EXIT procedure, foetal surgery, foetoscopy, intrauterine surgery

INTRODUCTION

Intrauterine surgery is becoming popular for treating foetal congenital anomalies.[1] This has provided many foetuses with significant anomalies to survive to full-term pregnancy and beyond.[2] Many factors have contributed to the success of this newly evolved field such as improvements in diagnostic and therapeutic technology, advances in understanding foetal pathophysiology, and the natural history of many of these conditions. Foetal intervention procedures include open foetal surgery, minimally invasive foetal surgery, *ex utero* intrapartum treatment (EXIT) procedures (intervention at caesarean delivery), foetal endoscopic surgery, and laser ablation of umbilical cords in twin pregnancies. An important consideration of intrauterine foetal intervention is that it should not jeopardise the safety of the mother. In most cases, foetal intervention is performed during pregnancy and pregnancy is continued to term. In some instances, EXIT surgery is performed on the foetus on placental support, followed by delivery. An understanding of maternal and foetal implications of anaesthetics is critical for optimum management of mother and foetus during foetal intervention. It is also critical to understand the physiological changes in pregnancy that influence anaesthetic management [Table 1]. Tables 2a and b summarise essential guidelines of anaesthetic management of a pregnant woman undergoing surgery.

Approximately over 1000 such cases are performed every year. This number is likely to increase in the future with advances in technology, attainment of foetal intervention skills, and enthusiasm to perform foetal interventions based on positive results of published data.

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Procedures amenable to foetal intervention

Table 3 lists indications of foetal interventions that are currently being performed. With further proficiency, new indications are forthcoming.[3-11] One of the most common indications is aortic valvoplasty in the foetus. This improves the growth and performance of the left ventricle at birth. Generally, each center of foetal intervention offers one or two procedures which may be considered their field of expertise.

Anaesthesia for minimally invasive procedures

The choice of anaesthesia depends on invasive procedure. Regional anaesthesia is the preferred technique where feasible. The impact of anaesthetic drugs on the foetus is minimal with regional anaesthesia. During our experience of over two decades, we have transitioned from general anaesthesia to regional anaesthesia for minimally invasive procedures [aortic valvoplasty, Table 4 and Figure 1].[12] General anaesthesia was a preferred technique during the earlier phase of our practice. This was based on the perception that uterine relaxation and foetal analgesia were essential requirements of foetal intervention.[12,13] Foetuses undergoing procedures at mid to late gestation may have the requisite neural development for pain and stress response.[14] Hormonal and haemodynamic stress responses do suggest that foetuses respond to noxious stimuli.[15,16] Therefore, foetal analgesia is a prime concern to be addressed during anaesthesia for foetal surgery. Although it was our belief two decades ago that uterine relaxation was necessary for minimally invasive surgery, such as aortic valvoplasty, experience over a decade suggests that uterine relaxation for minimally invasive procedures was not essential.

Table 1: Anatomical and Physiological Changes of Pregnancy

System	Changes
Cardiovascular system	Cardiac output increases 30%-50%, systemic vascular resistance decreases 30%, blood volume increases by about 50%
Respiratory system	Minute ventilation increases 40%-50%, oxygen consumption increases 20%-40%, function residual capacity is reduced 20%, normal $PaCO_2$ is 28-32 mmHg
Gastrointestinal system	Upward rotation of stomach, increased incidence of reflux due to progesterone
Haematologic system	Plasma volume increases more than red blood cell volume increases, most clotting factors increase
Renal system	Renal blood flow and glomerular filtration rate increases decreasing creatinine
Nervous system	Minimum alveolar concentration decreases by 30%-40%
	More extensive block after neuraxial anaesthesia
Anatomic	Weight gain and increased vascularity of mucus membrane

Table 2a: General anaesthesia in a pregnant patient

Position	Left or right uterine displacement
Premedication	Oral sodium citrate 30 mL
	Metoclopramide 10 mg intravenous
Induction	Rapid sequence propofol and succinylcholine
Ventilatory adjustments	Keep $PETCO_2$ 32-34 mmHg
Maintenance	Desflurane, sevoflurane, or isoflurane, fentanyl, oxygen in air, and muscle relaxants (vecuronium, rocuronium)
Haemodynamics	Blood pressure within 20% baseline through boluses of ephedrine or phenylephrine; noninvasive cardiac output is an additional adjuvant in monitoring

Table 2b: Regional anaesthesia in a pregnant patient

Epidural anaesthesia
Combined spinal epidural anaesthesia
Maintain blood pressures and cardiac output as close to baseline during the procedure

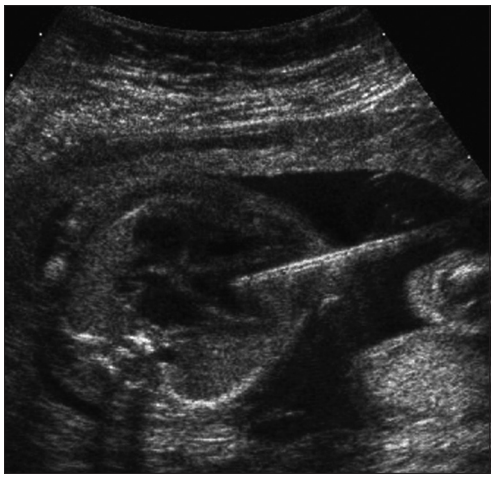

Figure 1: Ultrasound-guided needle placement into foetal left ventricle. A balloon catheter placed through the needle across the aortic valve to facilitate aortic valvuloplasty

Table 3: Intrapartum foetal interventions

Minimally invasive foetal surgery procedures
Twin-twin transfusion syndrome: laser ablation of blood vessels[9,10]
Obstructive uropathy: shunt insertion and valve ablation[3]
Aortic or pulmonary stenosis: valvuloplasty[11]
Cyanotic heart disease: atrial septostomy[8]
Congenital diaphragmatic hernia: tracheal balloon occlusion[4]
Spina bifida: fetoscopic closure of the malformation[5]
Twin reversed arterial perfusion: radiofrequency ablation[6]
Open foetal surgery
Myelomeningocele repair
Sacrococcygeal teratoma excision
Resection of intrathoracic masses
Congenital diaphragmatic - temporary tracheal occlusion
Congenital cystic adenoid malformation - excision

Table 4: Data from reference 12, 1999–2005

Cases by Year and Diagnosis

Year	Total cases	Cardiac	EXIT	Tracheal clip	Bladder shunt	TTTS
1999	2	0	1	1	0	0
2000	3	1	2	0	0	0
2001	9	2	6	0	0	1
2002	12	10	2	0	0	0
2003	20	14	2	0	2	2
2004	19	18	0	0	0	1
2005	24	21	1	0	0	2
Total	89	66	14	1	2	6

Anesthetic technique

Foetal anomaly	*n*	Intervention	GA	RA	GA + RA
Bladder obstruction	2	Shunt	0	2	0
Twin Transfusion	4	Cord ligation	2	2	0
Diaphragmatic hernia	12	EXIT	8	0	4
Restrictive Ventricle septum	8	Septostomy	6	0	2
Pulmonary stenosis	5	Balloon	3	0	2
Aortic stenosis	46	Balloon	28	0	18

EXIT – Ex utero intrapartum treatment; TTTS – Twin-twin transfusion syndrome; GA – General anaesthesia; RA – Regional anaesthesia

Moreover, administration of minimum alveolar concentration (MAC) over 1.5 can have depressant effect on the foetal myocardium. Administration of foetal intramuscular fentanyl (ultrasound-guided) can resolve the foetal pain concern. Foetal intramuscular injection of fentanyl along with a neuromuscular blocking agent ensures foetal immobility and foetal analgesia. Combined spinal epidural anaesthesia provides optimum conditions for minimally invasive procedures such as aortic valvoplasty. One milliliter of hyperbaric bupivacaine 0.75% with dextrose, with or without fentanyl 10 μg, provides an adequate level for foetal intervention. Left uterine displacement and monitoring of blood pressure are essential to maintain blood pressures within close limits of baseline. Recently, we have been using a noninvasive cardiac output device to continuously monitor cardiac output. The cardiac output data and blood pressure data provide valuable information while choosing the appropriate vasopressors [maternal intravenous (IV) phenylephrine and/or ephedrine]. Maintenance of maternal haemodynamics near normal values assures a steady cardiovascular state at the time of foetal intervention. Medications that may be used for foetal anaesthesia and immobility are fentanyl 10–50 μg/kg and vecuronium 0.1–0.3 mg/kg. Resuscitation medications for the foetus include epinephrine 1 μg/kg, and atropine 0.02 mg/kg. If foetal packed red blood cell transfusion becomes necessary, cytomegalovirus-free, leukocyte-depleted O-negative blood can be considered.[1,17]

Open foetal surgery

Surgery on the foetus is facilitated by a hysterotomy. An epidural can be placed before induction of general anaesthesia for providing postoperative pain relief. As an alternative, administration of a preoperative intrathecal opioid can be used. Both methods are equally efficacious in providing postsurgical pain relief. General anaesthesia by a rapid sequence induction, followed by maintenance of anaesthesia using inhalational anaesthetic agents, is a preferable technique as inhalational agents provide dose-dependent uterine relaxation necessary for optimum foetal surgical exposure.[18,19] Isoflurane, sevoflurane, and desflurane have been used successfully, although the latter two are more potent than isoflurane.[20] To prevent hypotension and foetal bradycardia, supplemental IV medications can be used in the initial stages of anaesthesia and inhalational agents are used when foetal exposure is required.[21] A two to three MAC concentration of inhalational agents is required for desired uterine relaxation and exposure. An arterial line will be helpful to monitor maternal blood pressure accurately. Central venous pressure monitoring is rarely required. Additional nitroglycerine boluses (50–100 μg IV) or infusion (0.5–1 μg/kg/min) can be used to supplement uterine relaxation, when inhalational agents are not sufficient. If neuraxial anaesthesia is being used for foetal surgery, IV nitroglycerine offers a good method to achieve uterine relaxation. However, this may be associated with maternal tachycardia, tachyphylaxis, methaemoglobinemia, headache, and pulmonary oedema.[22,23] Before uterine incision, placental position is ascertained. Uterine incision is made with a stapling device to prevent excessive uterine bleeding. The amniotic sac membranes are

sealed to the endometrium. Amniotic infusion with warm lactated Ringer's solution is used to maintain foetal temperature, maintain uterine volume, and avoid compression of umbilical cord.[23] Vasopressors are required to maintain blood pressure during the procedure because of vasodilatory effects of inhalational agents and/or nitroglycerine. Additional monitoring of cardiac output through arterial line is a good adjuvant in maintaining cardiovascular stability. Guarded administration of IV fluids is recommended to prevent maternal pulmonary oedema following foetal surgery. Foetal monitoring during the procedure can be achieved with pulse oximetry, continuous or intermittent echocardiography, foetal scalp electrodes, and umbilical blood sampling.[18]

Despite the transfer of inhalational agents from maternal to foetal circulation, which may be unpredictable, fentanyl for analgesia and muscle relaxant for foetal immobility can be administered intramuscularly to the foetus. Volatile anaesthetics can be discontinued or decreased soon after uterine closure. Anaesthesia can be maintained by propofol infusion. Maternal postoperative pain should be controlled with IV opioids. An intrathecal narcotic, if given prior to general anaesthesia, can adequately supplement analgesia to decrease postoperative pain. If an epidural is placed prior to general anaesthesia, epidural postoperative analgesia can be provided. Extubation should be performed with minimal coughing to avoid uterine dehiscence. Adequate postoperative pain control is associated with lower oxytocin concentrations in the blood, thereby decreasing premature uterine contractions.[24] Preoperative rectal indomethacin (50 mg) and postprocedure magnesium sulphate (4–6 g IV loading dose followed by 1–2 g/h IV infusion) are administered for tocolysis.[25] Terbutaline and nifedipine are used as supplements if above are ineffective.

EXIT (*ex utero* intrapartum treatment procedures)

This is also known as operation on placental circulation. The intervention can be performed with vaginal or caesarean delivery. The latter is preferable as it offers greater control and longer duration of placental support. Usually, these procedures are reserved for foetuses who are unable to oxygenate upon delivery due to airway abnormalities. An example of this is securing the baby's airway at the time of delivery, where the airway is compressed by a tumor (cystic hygroma), and while the baby is supported by the maternal circulation through umbilical cord [Figures 2 and 3]. EXIT

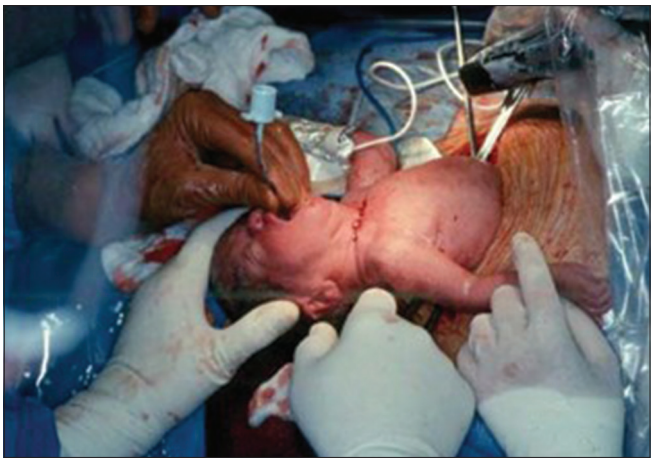

Figure 2: A foetus with a neck tumor. Airway being secured before disrupting uteroplacental–umbilical cord blood flow (EXIT)

procedures also facilitate transition to extracorporeal membrane oxygenation for oxygenation of the baby and maintaining on the system until cardiorespiratory anomaly is corrected and the baby can oxygenate well on its own. Once the oxygenation of the baby is assured without the need of maternal support, the baby is delivered from the uterus and umbilical circulation is terminated. Procedures involving longer than 2 h have been successfully performed using EXIT procedures.[26]

The majority of EXIT procedures are performed under general anaesthesia using high concentrations of volatile anaesthetics at the time of hysterotomy to facilitate uterine relaxation.[23] Uterine relaxation is essential for facilitating the controlled delivery of the foetal head and maintaining the placental circulation by preventing placental separation from the uterus. Vasoactive medications will be necessary to maintain blood pressure. Arterial blood pressure monitoring is preferable for titration of vasoactive medications. Cardiac output monitoring can provide additional data for choosing vasoactive medications. Maintaining maternal blood pressures and cardiac output closer to baseline ensures adequate placental blood flow.

The usual precautions of general anaesthesia for caesarean delivery apply to EXIT procedures. After the baby is delivered, uterotonics should be administered and inhalational agents are terminated. As the concentration of induction agents decrease, IV propofol can be administered for maintaining general anaesthesia. A Bispectral Index Monitor can assure adequate depth of anaesthesia for this transition and maintain optimal depth of general anaesthesia. Postoperative analgesia can be achieved through an

Figure 3: (a) Airway secured at EXIT procedure. (b) Surgical exicision of cystic hygroma

epidural route if there is a preexisting catheter. If not, systemic analgesics can be used. A transverse abdominal plane block can offer additional analgesia. Overall risk of haemorrhage is increased due to atonic uterus. Crossed match blood should be available for these procedures.

Foetoscopy procedures

Foetal endoscopic surgery ('Fetendo') obviates the need for a large uterine incision and may reduce the overall risks of foetal surgery by causing less uterine trauma and ultimately less preterm labor. In 1973, Schrimgeour introduced the term foetoscopy after exposing the uterus at laparotomy and inserting a 2.2-mm needle scope to view the amniotic cavity and foetus.[27] Foetoscopy surgery can be performed by two methods. In the first method, trocars are introduced into the uterine cavity through a laparotomy. In the second, less invasive method, a trocar is introduced percutaneously. Foetoscopy has since then adapted to many foetal interventions. Temporary tracheal occlusion is a promising strategy to enlarge the lungs in foetuses with congenital diaphragmatic hernia. Aberrant vessels leading to twin–twin transfusion syndrome can be ligated to prevent foetal death. Similarly, radiofrequency ablation or coagulation of nonviable twin's umbilical cord in twin reversed arterial perfusion, division of amniotic bands in amniotic band syndrome, and laser ablation of posterior urethral valves through foetal cystoscopy are other procedures undertaken using foetoscopy. A combined epidural spinal anaesthesia as described below with sedation is suitable for these procedures.

Mirror syndrome

Mirror syndrome is the development of maternal pulmonary oedema in the setting of severe foetal hydrops. These patients can present with preeclampsia-like symptoms which can make distinguishing between this condition and preeclampsia difficult.[7] The most common maternal symptoms are weight gain and maternal oedema (89.3%), followed by elevated blood pressure (60.7%), mild anaemia and haemodilution (46.4%), albuminuria and proteinuria (42.9%), elevated uric acid and creatinine (25%), mild elevated liver enzymes (19.6%), oliguria (16.1%), and headache and visual disturbances (14.3%). Severe maternal complications including pulmonary oedema occur in 21.4% of cases.[28] The average rate of intrauterine death and stillbirth is 35.7%, and the average time until maternal symptoms disappear is about 8.9 days.[28] The etiology remains unclear, but the maternal symptoms are reversible by successful foetal intrauterine therapy or, in certain cases with poor foetal prognosis, by foetal termination.[29] Foetal intervention includes placement of a peritoneal-amniotic shunt. This resolves the foetal hydrops and maternal mirror syndrome in some cases.[30] For foetoscopy procedures, anaesthesia is induced and maintained by combined spinal–epidural technique, with subarachnoid injection of administrations of 2.5 mg of bupivacaine and 25 mcg of fentanyl. Additional anaesthesia is provided through epidural catheter by administering 6–9 mL of 1%–2% lidocaine with epinephrine (1 in 200,000) or 0.25% bupivacaine, as required. This cautious approach prevents hypotension which may require fluid boluses, thus predisposing parturient to the risk for developing mirror syndrome (Ballantyne syndrome). Hence, it is prudent to avoid fluid overload in these patients undergoing foetal therapy.

Postoperative precautions

The foetal heart is closely monitored in the immediate postoperative period. The duration of monitoring depends on the nature of intervention and may extend to 24–48 h following open foetal intervention. Premature labour should be avoided with uses of tocolytics. Left

lateral tilt of the patients in the postoperative period and haemodynamics and oxygenation monitoring should be adopted. Venous thromboprophylaxis should be considered.

Complications

Apart from the complications related to anaesthesia for caesarean delivery, or interim nonobstetric surgery, there is susceptibility towards postoperative pulmonary oedema due to tocolytic use or foetal anomaly (hydrops foetalis). In addition, foetal surgery can predispose the mother to other potential maternal risks such as haemorrhage, premature rupture of membranes, chorio-amnion membrane separation, preterm labour, preterm delivery, foetal demise, chorioamnionitis, placental abruption, and increased need for maternal transfusion at the time of delivery.

SUMMARY

Foetal surgery requires a coordinated multidisciplinary approach. The benefit to the baby should be weighed against the risk to the mother. With advancements in technology and skill of interventional clinicians, many more foetal anomalies will be diagnosed *in utero* with proposed novel interventions. The temptation to undertake novel approaches will require careful evaluation of maternal risk. The anaesthetic approach must consider a technique that ensures maternal and foetal cardiovascular stability, sustained placental blood flow, minimal depression of foetal organ functions, foetal analgesia, foetal immobility, adequate blocking of the foetal stress response, and uterine relaxation during surgical procedure. For EXIT procedures, return of uterine tone is critical after delivery of the baby. International consensus from academic societies is guiding future strategies of management. For example, an international MOMs trial supports foetal repair of meningomyelocele for normal growth and function of neuraxial system in the foetus and beyond after delivery.[31]

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Conflicts of interest

There are no conflicts of interest.

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