Anaesthesia for Foetal Interventions

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KEY POINTS

- The 3 main types of foetal interventions include minimally invasive techniques, open foetal surgeries (requiring hysterotomy), and ex-utero intrapartum treatment.
- Minimally invasive and open foetal surgical procedures seek to prevent foetal demise and infant mortality and morbidity, whereas the ex-utero intrapartum treatment procedure allows foetal intervention to facilitate birth and transition to neonatal life.
- Management of uterine tone is crucial, especially in open midgestation procedures, to prevent preterm labour.
- A multidisciplinary team approach emphasizing maternal autonomy, support, and informed consent is essential for safe management.

INTRODUCTION

Anaesthesia for foetal surgeries has evolved alongside advances in prenatal diagnostics. Anaesthesiologists must consider 2 or more high-risk patients simultaneously, the pregnant patient and the foetus or foetuses. These interventions require specialized skills, a multidisciplinary team, and advanced infrastructure, often in quaternary centres.[1] The American College of Obstetricians and Gynaecologists and the American Academy of Paediatrics endorse dedicated foetal therapy centres with teams consisting of maternal-foetal medicine specialists, paediatric and obstetric anaesthesiologists, neonatologists, cardiologists, paediatric surgeons, radiologists, perioperative nurses, social workers, and geneticists.[2] The most common foetal interventions performed include laser ablation for twin-twin transfusion syndrome, myelomeningocele (MMC) repair, and procedures like foetoscopic endoluminal tracheal occlusion (FETO) and ex-utero intrapartum treatment (EXIT).

INDICATIONS FOR FOETAL INTERVENTIONS

The indications for the interventions can be categorized as follows:

- Improve the quality of life of the foetus (eg, foetal MMC repair has shown reduced incidence of hydrocephalus and improved motor development[3])
- Help the foetus transition to extrauterine life (eg, EXIT procedure for external airway compression)
- Correct congenital malformations to enable foetal survival (eg, FETO for congenital diaphragmatic hernia seems to increase neonatal survival in certain cases, although more work must be done to improve techniques and evaluate outcomes[4])
- Relieve parturients' symptoms (eg, in mirror syndrome, the parturient benefits from foetal treatment or delivery[5])

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TYPES OF FOETAL INTERVENTIONS

Foetal interventions are undertaken at early/midgestational age or birth. They are broadly classified as minimally invasive, open midgestation, and EXIT procedures. Common foetal conditions amenable to foetal procedures are shown in Table 1.

Minimally Invasive Procedures

These are performed at early or midgestational age and involve placing needles or fetoscopes through the abdominal wall and uterus to access the foetus, placenta, or umbilical cord.[6] Fetoscopes are small rigid endoscopes 1.0 to 3.8 mm in diameter with specialized working channels. Although some foetoscopic procedures might require laparotomy, no hysterotomy is involved, preserving the possibility of future vaginal delivery.[6]

Common needle-based procedures include foetal percutaneous umbilical blood sampling, intrauterine foetal blood transfusion, thoraco- or vesico-amniotic shunt placement, or radiofrequency ablation for sacrococcygeal teratoma (Figure 1). Examples of foetoscopic procedures include FETO and laser coagulation of vascular anastomoses causing twin-twin transfusion syndrome.

Open Midgestation Procedures

Typically performed at 24 to 26 weeks gestation, these procedures involve maternal laparotomy with hysterotomy to access the foetus. The uterus is exteriorised, and an incision of 6 to 8 cm is performed for the hysterotomy, making sure to avoid the placenta (identified using ultrasound). The possibility of vaginal birth is precluded both in current and subsequent pregnancies, as uterine contractions during labour can lead to uterine rupture.[6,7] Common procedures performed are repair of MMC and excision of sacrococcygeal teratoma or lung tumours.

Foetal Condition	Pathophysiology	Treatment	Type of Foetal Intervention
Twin reversed arterial perfusion	Monochorionic twins, normal twin supplies blood to acardiac twin	Radiofrequency ablation or cord coagulation of the acardiac twin	Minimally invasive
Twin-twin transfusion syndrome	Monochorionic twins, 1 twin is the blood donor (growth restricted), and other twin is the recipient (cardiomyopathy)	Amnioreduction Laser ablation of placental vessels, which cause unequal blood flow	Minimally invasive
Urinary tract obstruction	Obstruction in the urinary tract leading to pulmonary hypoplasia	Vesicoamniotic shunt or foetoscopic ablation of obstruction	Minimally invasive
Congenital diaphragmatic hernia	Pulmonary hypoplasia and hypertension due to hernia of the abdominal viscera into the thoracic cavity	Foetal endoscopic tracheal occlusion; prevents efflux of fluid from the lungs, improving pulmonary development	Minimally invasive
Amniotic band syndrome	Amniotic membrane bands tangle and restrict growth of different body parts	Release of bands using laser	Minimally invasive
Myelomeningocele	Spinal canal, meninges, and vertebrae do not fuse	Open or foetoscopic repair	Open midgestation or minimally invasive
Sacrococcygeal teratoma	Teratoma at the base of the coccyx that can cause high-output cardiac failure	Radiofrequency ablation; open tumor debulking	Minimally invasive
Selected cardiac conditions	Depends on specific lesion	Catheter-based balloon valvuloplasty or atrial septoplasty	Minimally invasive
Congenital cystic adenomatoid malformation	Intrathoracic tumours (cystic or solid) that compress the heart and cause foetal hydrops	Cyst drainage, shunt placement, or pulmonary lobectomy	Open midgestation
External airway compression	Compromised airway	Airway secured while on placental support	Ex-utero intrapartum treatment procedure

Table 1. Commonly Performed Foetal Procedures

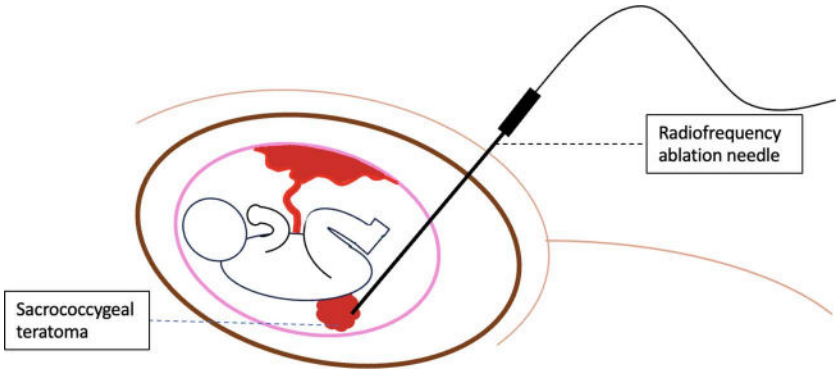

Figure 1. Radiofrequency ablation for sacrococcygeal teratoma. Radiofrequency ablation involves the precise application of heat to the feeding vessel of the tumour, interrupting blood flow to the sacrococcygeal teratoma, and shrinking or eradicating the teratoma. Radiofrequency ablation is a type of minimally invasive procedure.

EXIT Procedures

These interventions are conducted closer to term. After hysterotomy, foetal oxygenation is maintained via placental circulation, which gives the surgical team time to perform the intervention needed to allow the foetus to transition to extrauterine life. The specific interventions required to allow transition to extrauterine life will depend on the foetal pathology. For example, airway obstruction may require rigid bronchoscopy and intubation or neck dissection and retrograde wire intubation.[6,7] A large lung tumour may require thoracotomy and pulmonary lobectomy.[8] The foetus is delivered at the end of the procedure.

ANAESTHETIC CONSIDERATIONS

The choice of anaesthetic technique depends mainly on the parturient's gestational age, foetal concerns, and the type of procedure.

Maternal Physiology

Anatomical and physiological changes of pregnancy occur in response to the developing foetus's metabolic demands. In a supine patient, the gravid uterus compresses the inferior vena cava and descending aorta by 20 weeks gestation. Left uterine displacement alleviates supine hypotension and is recommended for procedures performed at the start of the second trimester.[9] Also, the onset of hypoxemia is faster during episodes of apnoea as functional residual capacity is reduced.[10]

Foetal Physiology

Understanding foetal physiology is essential to provide anaesthesia for foetal interventions. The foetal cardiovascular system forms a parallel circuit with over 50% of the placenta's blood volume (120 to 162 mL/kg). The total cardiac output (CO) is 425 to 500 mL/kg/min, with the right and left sides of the heart having dissimilar COs. Alterations in stroke volume exert minimal impact on CO due to the presence of noncontractile elements within the foetal heart and external compression exerted by fluid-filled lungs.[7] Hence, the CO is primarily dependent on heart rate changes. Foetal bradycardia is an important indicator of foetal stress.

Foetal pain physiology is complex and poorly understood. Thalamocortical connections develop around 23 to 30 weeks, which allows the foetus to experience pain beyond this stage. However, the foetal hypothalamic-pituitary-adrenal axis becomes active and produces β-endorphins and cortisol by 18 to 20 weeks.[6] Noxious stimuli trigger elevated cortisol and catecholamines, decreasing placental blood flow and causing foetal bradycardia. This prompts the redirection of blood to vital organs (the brain, heart, and placenta), termed the 'central sparing effect'. Thus, opioids are often administered during midgestation interventions (18 to 20 weeks) to mitigate potential stress responses, even though the foetus may not perceive pain at this stage.[6]

Placental Transport of Common Anaesthetic Drugs

The rate of drug transfer across the placenta depends on pharmacological factors (molecular weight, lipid solubility, protein binding, and concentration gradient) and placental factors (placental drug transporters, pH of maternal and foetal blood, surface area, thickness, and uteroplacental blood flow).[11] Table 2 shows the placental transfer of commonly used anaesthetics.

Anaesthetic Drugs	Rapid Placental Transfer	Notes
Volatile anaesthetics	Yes	High lipid solubility and small molecular size
Thiopental sodium	Yes	High lipid solubility and weak acidic nature
Propofol	Yes	High lipid solubility
Benzodiazepines	Yes	High lipid solubility in un-ionized form
Opioids	Yes	Less protein binding
Morphine		High lipid solubility
Fentanyl		Remifentanil is metabolised rapidly by nonspecific esterases; hence it does not lead to residual neonatal sedation.
Remifentanil		
Nondepolarising muscle relaxants	No	Large size, highly ionized and poor lipid solubility
Succinylcholine	No	Potential to transfer only in the setting of very high doses
Neostigmine	Yes	Small size (can transfer faster than glycopyrrolate and cause foetal bradycardia, so often recommended to combine with atropine for neuromuscular reversal)
Glycopyrrolate	No	Quaternary amine
Suggamadex	Minimal	Large size, polarised molecule
Dexmedetomidine	Yes	High lipid solubility
Atropine	Yes	Tertiary amine and lipid soluble
Local anaesthetics	Yes	Weak bases (in an acidotic foetus, may ionize after placental transfer leading to 'ion trapping'[12])

Table 2. Placental Transfer of Commonly Used Anaesthetics

PREOPERATIVE EVALUATION AND PLANNING

Multidisciplinary teams typically engage in patient care and counselling. It is essential to discuss with the parturient the potential outcomes, benefits, and risks, including maternal and foetal code status, particularly if the foetus is considered 'viable' at the time of the procedure (often >24 weeks gestational age; however, this may vary by location). Emphasis is placed on maternal autonomy, informed consent, and the provision of support services.[13]

The preoperative evaluation typically includes a thorough review of maternal comorbidities, including previous obstetric, surgical, and anaesthetic histories. A physical examination commonly focuses on airway assessment, screening for spinal conditions that may preclude neuraxial anaesthesia, and cardiopulmonary system assessment.[6] For minimally invasive procedures, a blood type and screen are usually sufficient. A blood type and cross-match are beneficial for open midgestation and EXIT procedures, as is the planning for massive transfusion. Other investigations are ordered as guided by history and examination.[13]

Foetal ultrasound, magnetic resonance imaging, and echocardiography are reviewed, and the extent of anatomical and physiological derangement is evaluated. Contraindications to foetal interventions, such as chromosomal abnormalities, microdeletions, or duplications, are typically ruled out by foetal genetic studies.[13] Emphasis is given to the baseline foetal heart rate, cardiac function, estimated foetal weight (for drug dosing), and placental position. Irradiated, leukocyte-reduced, O-negative blood cross-matched to the parturient is often readily available for the foetus.

Foetal Monitoring

The type of foetal intervention determines the monitoring requirements, which can vary from intermittent ultrasound monitoring of the heart rate to continuous echocardiography. During EXIT procedures, foetal pulse oximetry is monitored. Foetal oxygen saturation typically ranges between 30% and 70% due to low intrauterine oxygen tension.[6] It is highest in the umbilical vein (55 mmHg) and lowest in the umbilical artery (15 to 25 mmHg).[14] Figure 2 illustrates the foetal and maternal oxygen-haemoglobin dissociation curve. Foetal oxygenation takes place in the steep part of the oxygen-haemoglobin dissociation curve. Thus, even minor alterations in the partial pressure of oxygen can result in significant changes in foetal oxygen saturation. Factors such as vasoconstriction, uterine contractions, and potential sources of light interference can compromise the reliability of foetal oximeter readings.

Uterine Tone

Uterine contractions can result in increased uterine vascular resistance, umbilical cord compression, foetal bradycardia, and premature labour. Intraoperatively, profound uterine relaxation can be accomplished through the judicious use of

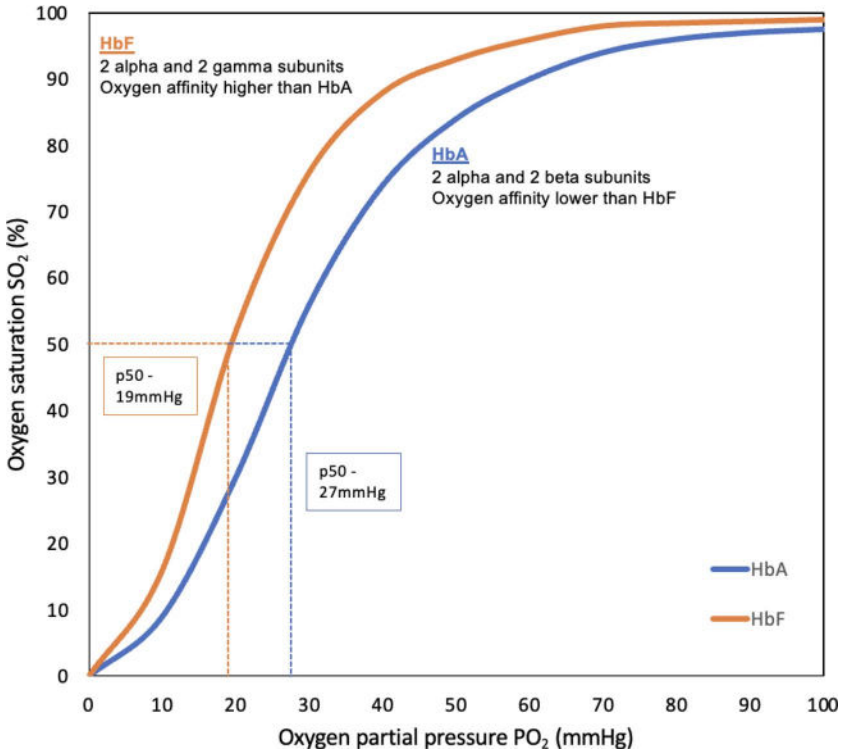

Figure 2. Foetal and maternal oxygen-haemoglobin dissociation curves. The foetal curve is shifted to the left as the foetus has higher affinity for oxygen. This allows the foetus to extract oxygen from maternal blood in the placenta, where oxygen levels are lower. Drop in PO_2 due to maternal hypotension, umbilical cord compression, or placental insufficiencies can lead to a drastic fall in foetal saturation. HbA Adult haemoglobin; HbF Foetal haemoglobin.

volatile anaesthetic agents, magnesium sulphate infusion, nitroglycerin, and beta-agonists. Uterine contractions can be triggered by the loss of uterine volume that occurs during hysterotomy. This is mitigated by continuous infusion of warmed crystalloid into the amniotic cavity, ensuring a warm environment for the foetus. In EXIT procedures, uterotonics are administered after foetal delivery.[6] Doses of commonly used tocolytics and uterotonics are outlined in Table 3.

Foetal Drug Administration

If required, drugs are administered to the foetus either indirectly by the anaesthesiologist via the transplacental route or directly by the surgeon (intravascular, intramuscular, or intracardiac). In the transplacental passage of drugs to the foetus, the

Tocolytics	Dose
Magnesium sulphate	4 to 6 g loading dose over 20 minutes followed by 2 to 4 g/h infusion
Volatile anaesthetics	2 to 3 MAC
Nitroglycerin*	50 to 100 mcg IV bolus, 0.5 to 3 mcg/kg/min infusion, 1 mg sublingual spray
Nifedipine	10 to 20 mg orally every 6 to 8 hours
Atosiban	6.75 mg IV bolus followed by 24 mL/h infusion for 3 hours
Indomethacin	50 to 100 mg PO or PR
Terbutaline	250 mcg IM or IV, 5 to 10 mcg/min IV
Uterotonics	**Dose**
Oxytocin	1 to 2 U IV bolus followed by infusion (7.5 to 30 U/h)
Carboprost	250 mcg IM every 15 minutes, maximum 8 doses
Methylergonovine	200 mcg IM, may repeat after 2 hours

Table 3. Tocolytics and Uterotonics. IM, intramuscular; IV, intravenous; MAC, minimum alveolar concentration; PO, orally; PR, rectally. *An infusion dose of up to 20 mcg/kg/min has been reported[15]

parturient might receive higher doses of drugs than the clinical anaesthetic requirement.[6] Fentanyl and remifentanil can be given via this route for maternal and foetal sedation and analgesia.[16]

Direct administration of drugs to the foetus offers the advantage of tailoring doses according to foetal needs while circumventing drug exposure to the parturient. Umbilical, hepatic, and peripheral veins are common sites of foetal intravascular access. Limitations of this approach include vasospasm of the umbilical vein cannulation, arrhythmia, and tamponade with intracardiac administration, leaving this approach largely for cardiac procedures. Intravascular routes are preferred for EXIT procedures.[6]

The shoulders and buttocks of the foetus are usually the sites of intramuscular drug administration, with drug volume limited to 0.2 to 0.5 mL.[6] In an unanaesthetised foetus, this can trigger a stress response that can cause the shunting of blood away from muscles and lead to unpredictable absorption. This route is usually used in minimally invasive or midgestation open procedures. The routes and doses of drugs commonly administered to the foetus for anaesthesia are summarized in Table 4.

ANAESTHETIC MANAGEMENT

Minimally Invasive Procedures

Anaesthetic management depends on the procedure, number, position, and size of the port site, the patient's position, and the requirement for maternal anxiolysis. Less invasive procedures, such as amnioreduction or percutaneous blood sampling, may not require an anaesthesiologist's involvement. For other procedures, the parturient can be sedated with careful use of opioids, benzodiazepines, dexmedetomidine, or propofol, avoiding loss of airway reflex. Neuraxial anaesthesia may be used for these procedures according to institutional preference. Intense uterine relaxation is generally not required, but tocolytics may be administered preoperatively. Maternal monitoring consists of standard American Society of Anesthesiologists monitors. Routine maintenance fluid is administered. Ephedrine or phenylephrine is used to mitigate maternal hypotension. In circumstances where complete foetal immobility is required, a combination of drugs (an opioid, a muscle relaxant, and an anticholinergic) is injected intramuscularly into the foetus. Most centres in North America administer a combination of fentanyl (20 mcg/kg), vecuronium (0.2 mg/kg), or rocuronium (2mg/kg) and atropine (20 mcg/kg) to the foetus.[6]

Open Midgestation Procedure

Although institutional preferences certainly impact plans, these procedures are commonly performed under general anaesthesia. A low thoracic epidural catheter can be inserted preoperatively. The epidural can be activated during abdominal closure to avoid hemodynamic instability intraoperatively while ensuring a smooth transition to extubation and postoperative analgesia. In addition to standard American Society of Anesthesiologists monitors, blood pressure is often monitored via an arterial line. The parturient is positioned in the left uterine displacement. The trachea is intubated by rapid sequence intubation. Two large intravenous accesses are generally recommended due to the potential for rapid blood loss. Fluid should be administered judiciously (500 to 1000 mL) to prevent pulmonary oedema.

Anaesthesia is usually maintained with volatile anaesthetics. Desflurane was commonly used in the past due to faster titratability, but many centres now use sevoflurane, which has a lesser environmental impact. Before hysterotomy, the volatile anaesthetic dose is carefully increased to provide profound uterine relaxation while trying to minimize its depressant effect on foetal cardiac function. Supplemental intravenous anaesthesia with remifentanil or propofol, nitroglycerin infusion, or early infusion of magnesium sulphate can be used along with volatile anaesthetic to reduce the volatile requirement.[6,7]

Hysterotomy is performed once adequate relaxation is achieved. Foetal weight-based doses of epinephrine and atropine should be readily available for resuscitation of the foetus. Warm crystalloid solutions are infused into the uterus. The

Drug	Route	Dose
Indirect (transplacental)		
Remifentanil	IV to parturient	0.1 to 0.2 mcg/kg/min
Fentanyl	IV to parturient	1 to 2 mcg/kg/h
Direct)		
Atropine	IM/IV	10 to 20 mcg/kg
Fentanyl	IM/IV	20 mcg/kg
Vecuronium	IM/IV	0.1 to 0.2 mg/kg
Rocuronium	IM/IV	2 mg/kg

Table 4. The Route and Dose of Drugs Commonly Administered to the Foetus for Anaesthesia. IM, intramuscular; IV, intravenous

foetus is positioned optimally within the uterus to prevent loss of uterine volume and safeguard against foetal hypothermia. Transplacental passage of drugs administered to the parturient intravenously will provide some foetal analgesia while the foetal procedure is performed. A combination of opioids, nondepolarizing muscle relaxant, and atropine can be administered as an intramuscular injection to the foetus to ensure immobility. Foetal heart rate, cardiac function, and ductal patency are monitored continuously using echocardiography. The team should be prepared for emergency delivery and neonatal resuscitation if needed.

After completion of the foetal procedure, the foetus is returned to the uterine cavity for closure. Volatile anaesthetics are decreased after uterine closure. Although evidence for the use of magnesium sulphate for tocolysis is mixed, it is commonly administered to the parturient as a bolus (6 g) followed by infusion (2 to 4 g/h) for the prevention of uterine contractions.[17] The choice of a tocolytic agent will depend on the institution and patient factors. Neuromuscular blockade is reversed completely, taking into account that magnesium sulphate can increase muscle weakness by augmenting the effects of neuromuscular blocking drugs. The epidural, if placed, is activated, and the parturient is extubated when fully awake.

EXIT Procedure

Anaesthetic management of EXIT procedures parallels that of open midgestation procedures, with a notable distinction: the necessity to restore uterine tone following foetal delivery.[13] Figure 3 illustrates the anaesthetic management of EXIT procedures. A fully equipped standby operating theatre is essential for potential emergency foetal delivery during the procedure. Figure 4 portrays hysterotomy and securing the foetal airway. Figure 5 depicts the position that might be taken by personnel and equipment for the EXIT procedure in the operation theatre.
These complex procedures may have to be performed as an emergency before the scheduled date. Mock drills and simulations are valuable tools for teams, particularly those with less experience. These exercises not only enhance the team's ability to plan effectively but also facilitate the establishment of clearly defined roles and the collaborative troubleshooting of any

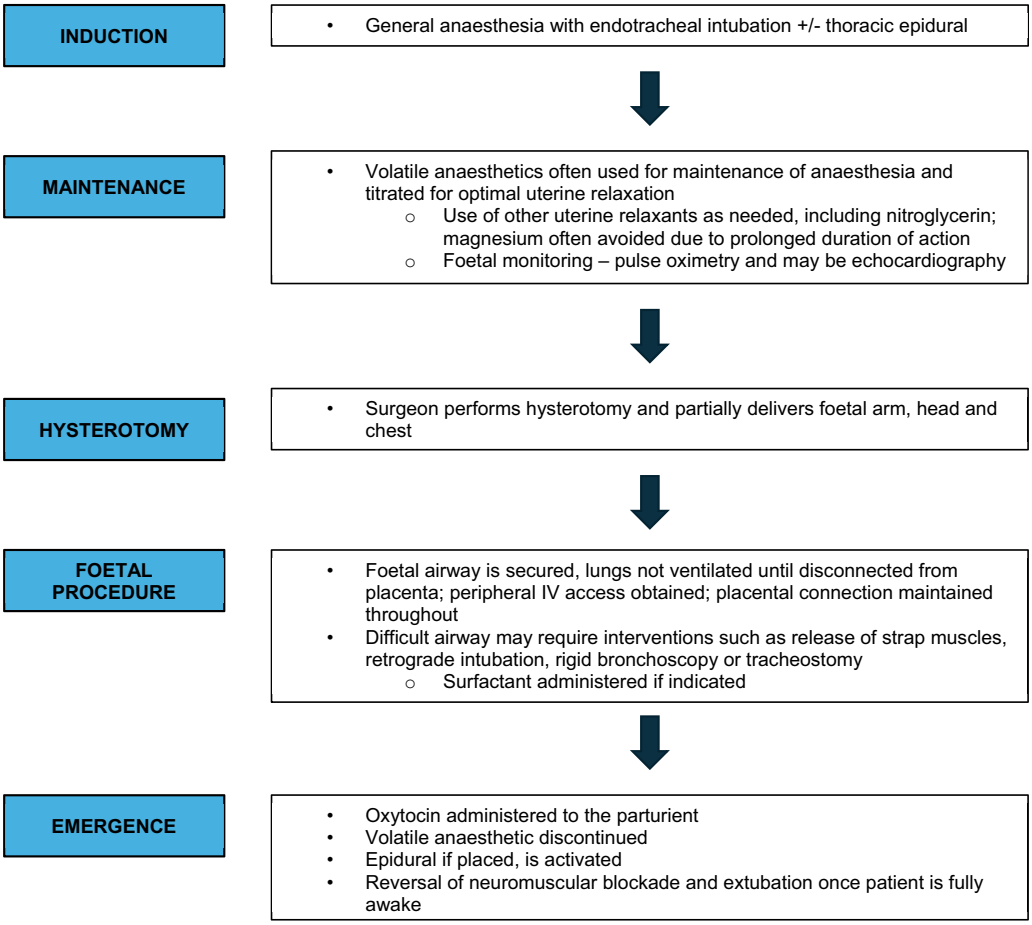

Figure 3. Anaesthetic management of ex-utero intrapartum treatment procedures. IV, intravenous.

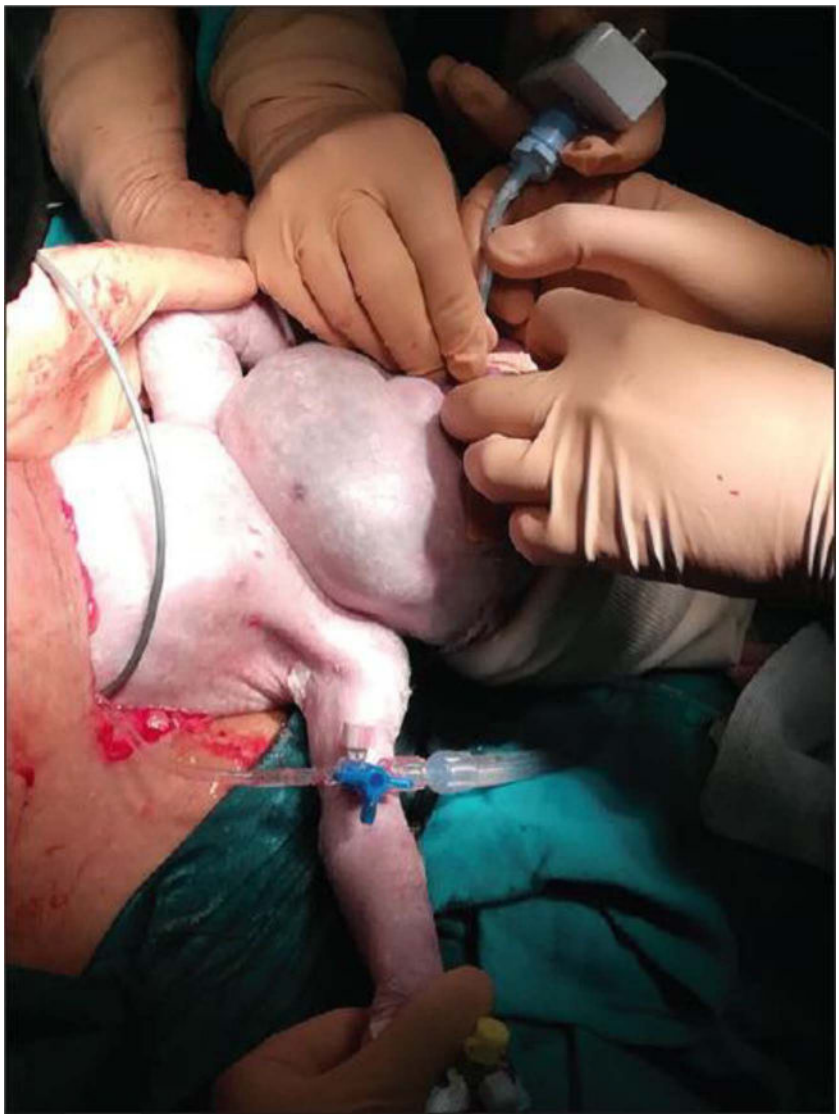

Figure 4. Ex-utero intrapartum treatment procedure. Hysterotomy and the securement of the airway in a foetus with large lymphatic malformation involving neck and upper mediastinum. Image obtained from Jain et al,[18] distributed under a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License.

challenges that may arise.[7] Because of the number of teams involved and the acuity of the situation, these procedures can be chaotic. The level of noise must be controlled, and the parallel workflows of all the teams must be carefully monitored and orchestrated.[7]

FOETAL RESUSCITATION

In situations of foetal instability, it may be necessary to pause the surgical procedure and perform foetal resuscitation. Indications and methods of resuscitation, along with causes of foetal bradycardia, are discussed below.

Indications for foetal resuscitation:

- Foetal bradycardia (foetal heart rate < 100 beats per minute)
- Foetal oxygen saturation of <30 to 40%
- Decreased cardiac filling
- Impaired ventricular function

Common causes of foetal bradycardia are summarized in Table 5.

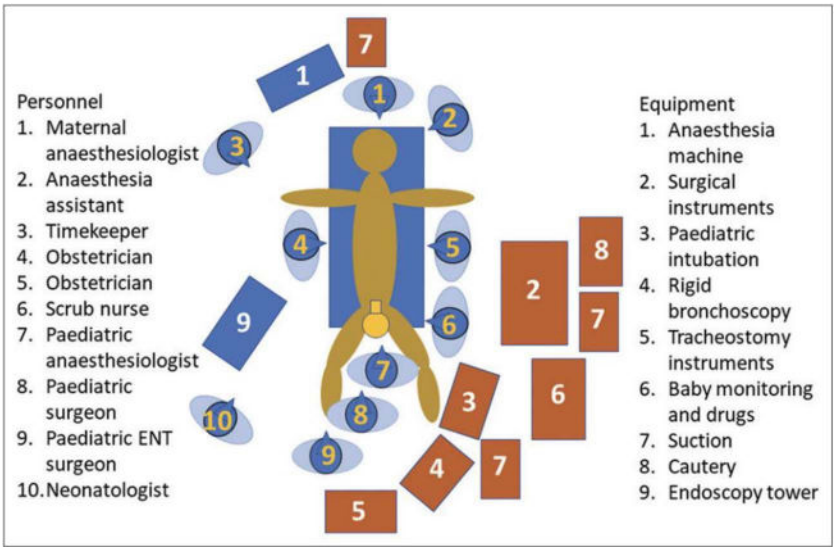

Figure 5. Possible arrangement of personnel and equipment in the operation room. ENT, ear, nose, throat. Image obtained from Nath et al,[10] distributed under a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License.

Resuscitation

- Consider increasing maternal-inspired oxygen
- Ensure left uterine displacement. Administer intravenous fluids and vasopressors to maintain maternal blood pressure and heart rate
- Improve uterine relaxation. Administer uterine tocolytics or increase the concentration of volatile anaesthetic
- Reposition the foetus to rule out umbilical cord compression
- Rule out placental abruption
- If bradycardia persists, the team can consider the following:
  - Give intramuscular epinephrine (10 mcg/kg) and atropine (20 mcg/kg) and intravenous fluids and blood
  - Perform foetal chest compressions at 100 to 150 bpm
  - If the foetus is viable, delivery and neonatal resuscitation
  - These tasks should be assigned to specific team members in preoperative team discussions.

MATERNAL AND FOETAL COMPLICATIONS

Parturients undergoing open midgestational procedures are at risk of premature rupture of membranes, preterm labour, and uterine rupture. Postpartum haemorrhage is a complication after EXIT procedures. Foetal risks include infection, oligohydramnios, intracranial haemorrhage, and intrauterine death.

POSTOPERATIVE MANAGEMENT

Postoperative management consists of monitoring, tocolysis, and pain management. It differs among procedures and is discussed in Table 6.

Most Common Causes	Less Common Causes
Kinking or mechanical compression of umbilical cord	Foetal hypovolemia
Placental separation	Foetal hypothermia
Uterine contractions	Foetal anaemia
Maternal hypotension	
Umbilical artery vasospasm	
Maternal anaemia	
Maternal hypoxaemia	

Table 5. Causes of Foetal Bradycardia

	Minimally Invasive	Open Midgestation	EXIT
Tocolysis	Generally not required	Required, magnesium sulphate (≥24 h) or indomethacin* may be used for tocolysis May need 48 to 72 h postoperative uterine monitoring	No tocolysis
Pain management	Oral analgesics generally sufficient for the parturient	Parturient may require epidural infusion of local anaesthetics and narcotics	Parturient may require epidural infusion of local anaesthetics and narcotics Neonate may need paracetamol or opioids depending on the procedure[19]
Maternal and foetal monitoring	Parturient may need monitoring for pulmonary oedema Foetal heart rate monitoring based on procedure, gestational age, and foetal condition	Parturient may need monitoring for pulmonary oedema Foetal heart rate monitoring and ultrasound tailored depending on procedure, gestational age, and foetal condition Caesarean section planned at 37 weeks gestation Steroids are administered to promote foetal lung maturity in cases of potential preterm delivery	Postoperative care mirrors that of a Caesarean section: pain management, thromboprophylaxis, and monitoring for bleeding

Table 6. Postoperative Management of Foetal Intervention Procedures. EXIT, ex-utero intrapartum treatment. *Indomethacin administration requires periodic foetal echocardiography to ensure patency of ductus arteriosus. Premature ductal closure can lead to persistent pulmonary hypertension of the newborn and foetal right heart failure[20]

SUMMARY

Anaesthetic techniques have evolved with developments in foetal interventions. Maintaining uteroplacental blood flow and volume, managing uterine tone, and minimizing maternal and foetal risks are key to providing anaesthesia for foetal interventions.

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