

Fetal Surgeries: A Newer Technique in Obstetrical Management

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Abstract

Fetal surgery is indicated in conditions which interfere with the normal development of the fetus, which when corrected will allow normal development of the fetus. Fetal surgeries can be performed in the form of open, fetoscopic, shunt therapy, radiofrequency ablation, fetal intracardiac catheter procedures and ex-utero-intrapartum-treatment (EXIT) procedures to correct various fetal anatomical defects. Examples of conditions treated by fetal surgeries include twin to twin transfusion syndrome (TTTS), congenital diaphragmatic hernia fetal tracheal occlusion, cystoscopic laser treatment of posterior urethral valves, and laser therapy of vocal cord occlusion in congenital high-airway obstruction sequence, and release of amniotic bands. In utero environment supports rapid post-operative healing, rapid healing, fostered by fetal growth factor, infections are combated by passage of maternal immune factors, umbilical circulation meets nutritional and respiratory needs without outside assistance and medical agents given directly to fetus have greater efficacy at reduced doses are the advantages of fetal surgeries over ex-utero surgical corrections. Over these advantages, there are challenges which have to be faced by the surgeons' are ethical dilemma, higher maternal and fetal risk, anesthesia risks, need for post-surgical tocolysis, fetal pain etc. It is not possible to assess fetal pain directly, assessed indirectly by ability of fetus to mount a stress response to noxious stimulus-increased fetal cortisol, beta-endorphins and central sparing hemodynamic changes. Fetal stress to pain starts in 8 weeks gestation age and may cause preterm labour. Researches are under the evaluation related to delivering stem cells or DNA to treat sickle cell anemia or other genetic conditions and inherited genetic diseases, prevention of graft v/s host disease and intra-amniotic or intra-umbilical vein.

Fetal surgical techniques using animal models were first developed at the University of California, San Francisco in 1980 by Dr. Michael R. Harrison and his research colleagues. On April 26, 1981, the first human open fetal surgery in the world was performed at University of California, San

Francisco under the direction of Dr. Michael Harrison. Further advances have been made in the years since this first operation. New techniques have allowed additional defects to be treated and for less invasive forms of fetal surgical intervention. The allure of Fetal Surgery is the possibility of

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interrupting the in utero progression of an otherwise treatable condition

Fetal Surgery is.....

- Indicated in conditions which interfere with the normal development of the fetus.
- Which when corrected will allow normal development of the fetus.

- It is contraindicated in conditions that are incompatible with life

- ✓ Severe affliction
- ✓ Other associated life threatening abnormalities
- ✓ Chromosomal and Genetic conditions

Table 1: Various in utero fetal malformations amenable to fetal surgery

Fetal structural defect	Natural fetal outcome	Recommended treatment
<ul style="list-style-type: none"> • Urinary tract obstructive defects ➤ Pelviureteric junction obstruction ➤ Ureterovesical junction obstruction ➤ Urethral obstruction ➤ Ureterocele 	<ul style="list-style-type: none"> Renal failure Renal failure hypoplasia Oligohydramnios 	<ul style="list-style-type: none"> Vesicocentesis Vesicoamniotic shunt Fetoscopic vesicostomy and laser ablation
<ul style="list-style-type: none"> • Lung defects ➤ Cystic adenomatoid malformation ➤ Pleural effusion ➤ Pulmonary sequestration 	<ul style="list-style-type: none"> Pulmonary hypoplasia Respiratory failure 	<ul style="list-style-type: none"> Pleuroamniotic shunt Thoracoamniotic shunt Open pulmonary lobectomy
<ul style="list-style-type: none"> • Diaphragmatic hernia 	<ul style="list-style-type: none"> Pulmonary hypoplasia 	<ul style="list-style-type: none"> Open complete repair Temporary tracheal occlusion
<ul style="list-style-type: none"> • Multiple pregnancy ➤ Twin-twin transfusion syndrome ➤ Acardiac twins 	<ul style="list-style-type: none"> Hydrops fetalis Intrauterine death 	<ul style="list-style-type: none"> Laser ablation Cord occlusion
<ul style="list-style-type: none"> • Sacrococcygeal teratoma 	<ul style="list-style-type: none"> Hydrops death 	<ul style="list-style-type: none"> Resection of tumor Radiofrequency ablation Fetoscopic vascular occlusion Cyst aspiration vascular occlusion
<ul style="list-style-type: none"> • Ovarian cysts • Placenta or amnion ➤ Chorioangioma of placenta ➤ Amniotic band syndrome 	<ul style="list-style-type: none"> Torsion Polyhydramnios Amputation of limb 	<ul style="list-style-type: none"> Ventriculoamniotic shunt Open ventriculo-peritoneal shunt Fetoscopic coverage Open repair
<ul style="list-style-type: none"> • CNS defects ➤ Aqueductal stenosis ➤ Dandy walker ➤ Myelomeningocele 	<ul style="list-style-type: none"> Brain damage Paralysis 	<ul style="list-style-type: none"> Fetoscopic coverage Open repair
<ul style="list-style-type: none"> • Facial defects ➤ Cleft lip and palate 	<ul style="list-style-type: none"> Facial deformity 	<ul style="list-style-type: none"> Fetoscopic coverage Open repair

Fetoscopic Surgery

Fetoscopy compares to open fetal surgery as laparoscopy does to laparotomy. To perform surgery using fiberoptic endoscopes only 1 to 2 mm in diameter and instruments such as lasers that fit through 3 to 5 mm cannula has revolutionized treatments available for selected fetal conditions. Risks are lower than with open fetal surgery but can still be formidable. Other risks include maternal infection or injury and fetal death.

Examples of conditions treated by fetoscopy include twintwin transfusion syndrome (TTTS), congenital diaphragmatic hernia fetal tracheal occlusion, cystoscopic laser treatment of posterior

urethral valves, and laser therapy of vocal cord occlusion in congenital high-airway obstruction sequence, and release of amnionic bands.

Twin-Twin Transfusion Syndrome (TTTS)

Laser therapy for TTTS has been the most commonly used example of fetoscopic surgery. With this procedure, laser energy ablates pathological vascular anastomoses within a monochorionic twin placenta. Even with such therapy, evaluation and management of TTTS remains challenging (Norton, 2007). For example, the relationship between placental angioarchitecture and pregnancy outcome

Table 2: Types of Fetal Surgeries

Surgery	Correction
Open Fetal Surgery	<ul style="list-style-type: none"> • Cystic adenomatoid malformation • Extralobar pulmonary sequestration • Sacrococcygeal teratoma
Fetoscopic Surgery	<ul style="list-style-type: none"> • Spina bifida • Twin-twin transfusion: laser of placental anastomoses • Diaphragmatic hernia: fetal endoscopic tracheal occlusion (FETO) • Posterior urethral valves: cystoscopic laser • Congenital high airway obstruction: vocal cord laser
Percutaneous Procedures	Amniotic band release
• Shunt therapy	Posterior-urethral valves/bladder outlet obstruction
• Radiofrequency ablation	Pleural effusion: chylothorax or sequestration
• Fetal intracardiac catheter procedures	Dominant cyst in congenital cystic adenomatoid malformation (CCAM)
Ex-utero-intrapartum-treatment(EXIT) procedures	Twin-reversed arterial perfusion (TRAP) sequence
	Monochorionic twins with severe anomaly(ies) of 1 twin
	Chorioangioma
	Aortic or pulmonic valvuloplasty for stenosis
	Atrial septostomy for hypoplastic left heart with restrictive atrial septum
	• Congenital diaphragmatic hernia after FETO
	• Congenital high airway obstruction sequence (CHAOS)
	• Severe micrognathia
	• EXIT-to-resection
	Resection of fetal thoracic or mediastinal mass
	Tumors involving airway/neck
	• EXIT-to-extracorporeal membrane oxygenation (ECMO)
	Congenital diaphragmatic hernia (if no fetal surgery)

is not fully understood, and neurological complications and preterm birth remain common. Treatment is even less likely to be successful in pregnancy after 26 weeks (Crombleholme and colleagues, 2007).

Fetal Endoscopic Tracheal Occlusion (FETO) for Congenital Diaphragmatic Hernia (CDH) Fetoscopic therapy has been rigorously evaluated in infants with this condition. With an isolated diaphragmatic hernia and with specialized care and postnatal surgery, mortality rates approximate 30 per cent (Reickert and colleagues, 1998).

Percutaneous Procedures

Sonographic guidance can be used to permit therapy with a shunt, radiofrequency ablation needle, or angioplasty catheter. Although risks are lower than with open fetal surgery, risks include maternal infection, preterm labor or prematurely ruptured membranes, and fetal injury or loss.

Fetal Shunt Therapy

Percutaneous shunts have been used to drain fluid in cases of selected urinary and thoracic abnormalities.

Urinary shunts are primarily used in cases of fetal bladder outlet obstruction for example, posterior urethral valves, that would otherwise be lethal. The rationale is that allowing urine to drain from the bladder into the amniotic cavity might preserve renal function and protect against pulmonary hypoplasia

from oligohydramnios. Only male fetuses are treated because in females the type of anomaly tends to be even more severe. One third of surviving children required dialysis or renal transplantation.

Thoracic shunts from the fetal pleural cavity into the amniotic cavity are performed to drain large pleural effusions. These may accrue with a chylothorax, or they may accompany pulmonary sequestration. Shunts have also been used to drain a dominant cyst in fetuses with congenital cystic adenomatoid malformation.

Radiofrequency Ablation Procedure (RFA)

With this procedure, high-frequency alternating current is used to coagulate and desiccate tissue. Recently this has become a favored modality for the treatment of twin-reversed arterial perfusion (TRAP) sequence or acardiac twin. It is also used for selective termination for other monochorionic twin complications. Without treatment, the mortality rate for the normal or pump twin in TRAP sequence exceeds 50 per cent, and it is even higher with larger acardiac twins.

Fetal Intracardiac Catheter Procedures

Selected fetal cardiac lesions are concerning because of their progression during gestation. For example, severe fetal aortic stenosis detected in the early second trimester may progress to a hypoplastic left heart by the third trimester (Simpson and Sharland, 1997).

Ex Utero Intrapartum Treatment (EXIT)

This procedure is designed to allow the fetus/ infant to remain perfused by the placental circulation after being partially delivered so that life-saving treatment can be performed prior to complete delivery. EXIT procedures have been performed for more than 15 years. The technique has also been used to treat airway obstruction caused by neck masses and laryngeal or tracheal atresia or stenosis (Steigman and associates, 2009). More recently, Kunisaki and co-workers (2007) used the EXIT procedure as a bridge to extracorporeal membrane oxygenation (ECMO).

Advantages of fetal surgery

- In utero environment supports rapid post-operative healing
- Rapid healing, fostered by fetal growth factor
- Infections are combated by passage of maternal immune factors
- Umbilical circulation meets nutritional and respiratory needs without outside assistance
- Medical agents given directly to fetus have greater efficacy at reduced doses

Challenges before the field of fetal surgery

- Ethical dilemma
- Maternal risk
- Fetal risk
- Maternal anaesthesia
- Fetal anaesthesia
- Post-surgical tocolysis

Ethical considerations and dilemma

- Not all procedures are performed regularly
- The results are not guaranteed
- Risk to both mother and fetus
- Psychological and neuro developmental consequences of fetal surgery
- Fetus is sacrificed to improve the outcome of in utero sibling
- Ethical dilemma-should a procedure which is not guaranteed to produce results be performed on the insistence of mother

Maternal Risks

- Tocolytic therapy can cause pulmonary edema

- Subsequent delivery by LSCS
- Intra operative blood loss
- Amniotic fluid leak
- Wound infection
- Intra uterine infection
- "Maternal Mirror Syndrome" in cases of fetal Hydrops
- Chorioamnionic membrane separation
- Deep anaesthesia is required to provide with adequate uterine relaxation for fetal manipulation and to prevent PT labor

Fetal Risks

- Prematurity
- Intra Uterine Infection
- Fetal vascular embolic events
 - ✓ Intestinal atresia
 - ✓ Renal agenesis
- Premature closure of Ductus Arteriosus
- CNS injuries due to maternal hypoxia or fetal circulatory disturbance

Anaesthesia for fetal surgery-basic considerations

- Pre-operative evaluation and preparation
- Relief of anxiety
- Avoidance of fetal asphyxia
- Adequate analgesia
- Uterine relaxation
- Prevention of preterm labour
- Maternal safety
- Avoidance of teratogenic agents
- Fetal anaesthesia and monitoring

Pre-operative evaluation

- Counseling of family
- Assessment of mother for fitness for anaesthesia
- Assessment of fetus

Pre-operative preparation

- Consent for caesarean delivery
- Maternal blood cross matched
- Availability of O-negative, cross matched blood against the maternal antibodies

- Indomethacin rectal suppository for postoperative tocolysis
- Epidural catheter for postoperative pain control

Fetal anaesthetic considerations

- Fetal organ systems are immature
- Fetal cardiac output is sensitive to HR changes
- Fetus has high vagal tone and thus response to stress with precipitous bradycardia
- Fetal circulatory blood volume is low, hence little intra-operative bleeding can cause hypovolemia, so trigger for transfusion is low.
- During prolonged surgery, fetus needs to be transfused O-negative blood.
- Hypothermia can be minimized by limiting fetal surgical time and use of warm irrigating fluids (37-38°C).
- Immature coagulation system predispose to bleeding and difficulty in hemostasis

Fetal pain

- Not possible to assess fetal pain directly
- Assessed indirectly by ability of fetus to mount a stress response to noxious stimulus-increased fetal cortisol, beta-endorphins and central sparing hemodynamic changes
- Fetal administration of narcotic inhibits cortisol and beta-endorphin release but does not inhibit central sparing hemodynamic changes
- Fetal stress to pain starts in 8 weeks gestation age and may cause preterm labour

Postsurgical tocolysis

- High risk of preterm labour
- Pre-operative: rectal indomethacin
- MgSO₄ is tocolytic of choice and maintained for 2-3 days-3 gm./hr. infusion
- Adequate maternal analgesia as maternal pain can cause preterm labour and fetal distress
- Epidural analgesia (PCEA) for 24-48 hrs. is recommended to prevent uterine contractility

Future possibilities

- Deliver stem cells or DNA to treat sickle cell anemia or other genetic conditions

- Inherited Genetic Diseases Treatable with Stem Cells
- Inherited Genetic Diseases Treatable with Stem Cells
- Prevention of graft v/s host disease
- Prevents further damage to the fetus
- Intra-amniotic or Intra-umbilical vein

New researches

- Remifentanyl produces improved fetal immobilization with good maternal sedation and only minimal effects on maternal respiration (AnesthAnalg, 2005).
- Continuous fentanyl infusion with midazolam provides acceptable maternal analgesia and sedation during fetoscopy (Masui, 2008).
- In fetoscopic interventions under GA, cardiopulmonary functions remain stable. However, a moderate increase in extravascular lung water (EVLW) and pulmonary vascular permeability indicates an increased risk for maternal pulmonary edema (Br J Anaesth, 2009).

“The key in fetal surgery is not when to operate, but to know when NOT to operate”

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