

## REVIEW ARTICLE

# Initial experience with the anaesthetic management of fetoscopic spina bifida repair at a German University Hospital

## *A case series of 15 patients*

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Spina bifida aperta (SBA) is a serious neural tube defect that can lead to a range of disabilities and health complications in affected individuals. In recent years, fetoscopic surgical repair has emerged as a promising new approach to treat spina bifida prenatally, offering the potential for improved outcomes compared with traditional open surgery. As one of the few centres in Europe to offer this innovative technique, the Departments of Obstetrics and Gynaecology, Neurosurgery,

and Anaesthesiology and Intensive Care Medicine at the University Medical Centre of Marburg (UKGM Marburg) have faced unique challenges in developing and establishing standards of care for the pregnant patients undergoing this complex procedure. In this publication, we aim to present details of our initial experience with the first 15 patients and propose a clinical concept for the rather complex perioperative management of these patients.

### KEY POINTS

- Spina bifida aperta is a serious malformation of the central nervous system and patients benefit from prenatal surgical closure of the defect.
- This surgical procedure has recently been commenced at our institution and has required developing a well thought out anaesthetic plan to be able to safely provide general anaesthesia for mother and foetus.
- Delivering anaesthesia to mother and foetus for this procedure is complex and requires knowledge about general anaesthesia during pregnancy as well as about foetal anaesthesia and physiology.
- Maintenance of utero-placental perfusion, foetal haemodynamic stability, anaesthesia for the foetus

and prevention of maternal postoperative pulmonary oedema are major concerns, which need to be addressed.

- In this publication, we present our plan for anaesthesia and the peri-operative management of these patients as a case series of the first 15 patients.

### Introduction

#### Spina bifida aperta

Spina bifida aperta (SBA) is a congenital, nonlethal malformation of the central nervous system caused by an incomplete closure of the neural tube during embryonal development. Myelomeningocele is a cystic form of SBA whereas myeloschisis is a more severe form with a

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commonly flat and open lesion.<sup>1</sup> The prevalence in Europe is about 4.9 per 10 000 births.<sup>2</sup>

Children with SBA are often in need of care because of muscle weakness or paralysis below the segment of the lesion as well as a neurogenic bladder or bowel dysfunction. Often patients develop hydrocephalus with the need for ventricular–peritoneal shunting. Commonly an Arnold–Chiari II malformation with herniation of parts of the cerebellum and brain stem is present.<sup>3</sup>

The 2011 ‘MOMS-Trial’ showed a significant advantage for the intra-uterine repair of myelomeningocele compared with the standard postnatal approach. The study found a significant reduction in the necessity for shunt placements in these patients at the age of 12 months as well as a significantly improved motor function at 30 months of age.<sup>4</sup>

The improved outcomes of the trial<sup>4</sup> are thought to be because covering the defect prenatally prevents progressive neuronal tissue damage caused by the neurotoxic amniotic fluid, and a reduction in mechanical pressure.<sup>4,5</sup>

### Surgical approaches for the intra-uterine repair of spina bifida aperta

For the intra-uterine repair of SBA, different surgical procedures have been established in the very few specialised centres around the world. A common approach is the open surgical technique, consisting of a transverse laparotomy and hysterotomy, as performed for the MOMS-Trial. This technique, however, leads to increased preterm birth rates and carries a risk of uterine dehiscence at delivery, which makes caesarean delivery obligatory.<sup>5,6</sup>

Newer surgical techniques use fetoscopic approaches, which are performed either fully percutaneously or as a laparotomy-assisted ‘hybrid’ procedure.<sup>7,8</sup> The hybrid method consists of a transverse laparotomy and fetoscopic access through the uterine wall to the foetus. The defect is covered in three layers consisting of a bovine dura patch, muscles and skin. In comparative clinical studies, a fetoscopic approach showed similar results to the open technique regarding foetal outcome. Additionally, uterine scarring is avoided and thus the risk of ruptured membranes, preterm delivery and uterine dehiscence is reduced, allowing for vaginal delivery.<sup>9,10</sup>

The development and implementation of the procedure at our institution has taken 2 years under the guidance of the ‘International Fetoscopic Myelomeningocele Repair Consortium’.<sup>11,12</sup> Experienced surgeons and anaesthesiologists from the Texas Children’s Hospital at the Baylor University in Houston, USA as well as surgeons from Leuven, Belgium consulted during the first procedures at our centre.

The surgical steps of the hybrid surgical technique are outlined in Table 1.

**Table 1** Surgical steps of the hybrid technique

1. Lower abdominal transverse laparotomy
2. Exposure of the uterus
3. Sonographic identification of placental edges
4. Introduction of a trocar in the uterus and partial drainage of amniotic fluid
5. Infiltration of CO <sub>2</sub> in the uterus
6. Introduction of two additional trocars
7. Preparation and mobilising of skin and muscles around the lesion
8. Insertion of a dura patch
9. Closure of muscle and skin above patch and lesion
10. Removal of the CO <sub>2</sub> and refilling of the uterus with Ringer’s acetate
11. Removal of the trocars and closure of uterus
12. Closure of maternal abdomen

### Preoperative care and preparations for surgery

Interdisciplinary presentation of the patient is performed before surgery.

An 18-gauge intravenous cannula is inserted and all patients receive the tocolytic atosiban, beginning on the day before surgery: a loading dose of 6.75 mg, then 54 mg over 3 h, followed by 100 µg min<sup>-1</sup> for 48 h.

On the day of surgery, a magnesium sulphate infusion (2 g h<sup>-1</sup>) is started in the morning and continued until the end of the procedure. Maternal premedication with oral midazolam (7.5 mg), and 30 ml of sodium citrate to buffer gastric acid are given 30 min before surgery.

Foetal drug dosages are calculated according to the current foetal weight as estimated by ultrasound. The medications are drawn up in sterile fashion into 1 ml syringes in a distraction free environment. The syringes are marked with coloured caps, for example, yellow for the analgesic mixture, and are placed in three kidney basins to enable differentiation of the medications (Table 2 and Fig. 1). Fentanyl, cisatracurium and atropine are drawn up together into one syringe to allow for easy administration of these medications to the foetus. Foetal drugs are administered intramuscularly through a long needle by the surgeon.

### Intra-operative management

#### Induction of anaesthesia

Before induction of general anaesthesia, a lumbar epidural catheter is placed at level L3/4 or L4/5 with the mother in a sitting position.

Induction of general anaesthesia is performed as a modified rapid sequence induction (RSI) using fentanyl (3 µg kg<sup>-1</sup>), propofol (2 mg kg<sup>-1</sup>) and rocuronium (1 mg kg<sup>-1</sup>) and the airway is secured with an endotracheal tube. A gastric tube, two additional peripheral intravenous cannulas (16 or 17 gauge) and an arterial line are then inserted. These additional intravenous cannulas are used for the various drug infusions, and as a backup should the initial cannula become unusable.

Patients are placed in the lithotomy position with the left arm extended out at 90° to the body and the right arm is padded and tucked alongside the body. The atosiban and magnesium infusions are administered for tocolysis

Table 2 Medications prepared for intramuscular injection to the foetus

	Dose per kg	Drug concentration	Cap colour (Fig. 1)
Analgesic mixture drawn up into one syringe			Yellow
Fentanyl	10 µg kg <sup>-1</sup>	50 µg ml <sup>-1</sup>	
Cisatracurium	0.6 mg kg <sup>-1</sup>	2 mg ml <sup>-1</sup>	
Atropine	0.03 mg kg <sup>-1</sup>	0.1 mg ml <sup>-1</sup>	
Resuscitation medications			
Epinephrine	0.01 mg kg <sup>-1</sup>	0.01 mg ml <sup>-1</sup>	Red
Atropine	0.03 mg kg <sup>-1</sup>	0.1 mg ml <sup>-1</sup>	Blue
Individual medications			
Fentanyl	10 µg kg <sup>-1</sup>	50 µg ml <sup>-1</sup>	Red
Cisatracurium	0.6 mg kg <sup>-1</sup>	2 mg ml <sup>-1</sup>	Blue

continuously during surgery. Cefazoline (1000 mg every 6 h) is given as peri-operative antibiotic prophylaxis and dexamethasone (4mg) and granisetron (1 mg) are given to help prevent postoperative nausea and vomiting.

Maintenance of anaesthesia and intra-operative homeostasis

For maintenance of anaesthesia and additional uterine relaxation, sevoflurane is used. Analgesia is provided

using intermittent doses of fentanyl or a low-dose remifentanyl infusion. To avoid hypotension, during the procedure, the epidural is only started towards the end of surgery to facilitate pain-free emergence from anaesthesia and recovery from surgery.

Epinephrine (10 µg ml<sup>-1</sup>), norepinephrine (10 µg ml<sup>-1</sup>) and nitroglycerine (0.5 mg ml<sup>-1</sup>) are prepared and connected and used as continuous infusions as and when required.

FIGURE 1 This photograph shows the prepared drugs for foetal analgesia as well as for maternal resuscitation in the respective kidney basins.



The A4 paper labels state the medications and dosages used as well as showing the calculated dosages using the current foetal weight added in green. The left basin contains the analgesic mixture for the foetus in syringes with a yellow cap: this consists of fentanyl (10 µg kg<sup>-1</sup>), atropine (30 µg kg<sup>-1</sup>), cis-atracurium (600 µg kg<sup>-1</sup>). The middle basin holds maternal resuscitation drugs as stated on the A4 label: epinephrine (10 µg kg<sup>-1</sup>) with a 10 µg ml<sup>-1</sup> solution (red caps) as well as atropine (30 µg kg<sup>-1</sup>) in syringes with blue caps. In the right kidney basin, we keep individual drugs for the mother, which are fentanyl (10 µg kg<sup>-1</sup>) with red caps and cis-atracurium (600 µg kg<sup>-1</sup>) with blue caps.



After induction, the crystalloid intravenous fluid is replaced by a slow infusion of a 5% albumin solution. Unless anuria occurs, or excessive urine output causes markedly negative fluid balance, or volume therapy is required to replace blood loss, fluid replacement is limited to  $10 \text{ ml kg}^{-1}$ . We target a fluid balance of 0 to  $-500 \text{ ml}$  during surgery. To preserve adequate utero-placental perfusion and homeostasis for the foetus, the maternal mean arterial pressure is kept within 10% of baseline values using vasopressors as necessary.

The foetal heart rate (FHR) is monitored every 10 to 15 min using Doppler sonography of the heart or umbilical cord. If a decreasing FHR is detected maternal blood pressure, oxygenation and temperature are immediately checked and corrected if not within normal limits. In the case of uterine contractions, sevoflurane concentration is increased up to 1.2 to 1.5 minimal alveolar concentration (MAC).

Ventilator settings are set to target normal maternal oxygenation and a  $\text{PaCO}_2$  value of  $30 \text{ mmHg}$ .

Normothermia is maintained as hypothermia can cause stress and haemodynamic compromise in the foetus. The operating room is heated to  $24^\circ\text{C}$ , the patient is placed on an electrical warming mattress and a forced air warming over-blanket is also used. Heated  $\text{CO}_2$  is used for uterine insufflation and the uterus is covered with a transparent plastic film as soon as all trocars are in place (Fig. 2).

#### Specific anaesthesiologic aspects

For secure placement of the uterine trocars, increasing the sevoflurane concentration up to 1.2 MAC provides adequate uterine relaxation. When uterine manipulation is stopped, the inhalational anaesthetic is reduced to lower levels (0.7 to 0.9 MAC). To ensure adequate maternal anaesthesia, bispectral index monitoring is used.

**FIGURE 2** This photograph shows an intra-operative view.



The uterus has been exposed and at the time of the photograph, the first incision into the uterus is made to introduce one of three trocars (surgeon on the right). The surgeon in the middle holds the uterus in place and stabilises the position of the foetus. On the left is the sonographer, responsible for measuring the foetal heart rate in 10-min intervals. Here the ultrasound is also used to ensure that the incision can be done safely without causing injury to the foetus or the placenta. After all trocars are in place, the uterus will be covered with a transparent film, which helps to keep the uterus warm.

Before any foetal surgical manipulation, the first dose of the analgesic mixture (opioid, NMBD, atropine, i.e. syringes with yellow cap in Fig. 1) is administered by the surgeon, which is then repeated hourly.

When the surgery on the foetus is completed, the previously aspirated volume of amniotic fluid is replaced by warmed Ringer's acetate solution in equal volume together with an antibiotic (clindamycine 600 mg).

Then trocars are removed, and the uterus is closed. During this part of the surgery, sevoflurane is increased again up to 1.2 MAC to prevent uterine contractions.

When the uterus is placed back in the abdomen, sevoflurane is reduced and a bolus of 10 µg of sufentanil in 10 to 15 ml of ropivacaine 0.2% is injected slowly through the epidural catheter, with careful monitoring of the maternal blood pressure as the combination of restrictive fluid therapy and sympathicolysis can lead to a marked fall in blood pressure.

Before emergence from anaesthesia, any residual neuromuscular block is reversed to a TOF-Ratio of at least 0.9 using neostigmine and atropine. When the patients are sufficiently awake, the trachea is extubated and the patients are transferred to an intermediate care unit.

### Postoperative care

The patient's vital signs are monitored for at least 48 h, and foetal monitoring is continued with ultrasound and CTG. To reduce the risk of postoperative pulmonary oedema, oral fluid is limited to 1500 ml per day. Urine output is closely monitored, and a balanced fluid input and output is targeted. Lung ultrasound can be used to detect pulmonary oedema.

The epidural catheter is kept until the fifth or sixth postoperative day, depending on the patient's needs. Additionally, oral oxycodone/naloxone and paracetamol are administered.

Patients are discharged from hospital 6 to 10 days after surgery but are followed up regularly until delivery.

## Results

### Case series of the first 15 cases

In this article, we present the first 15 patients undergoing the fetoscopic spina bifida surgery procedure at our institution.

Our patients were between 19 and 38 years old and came with a diagnosis of foetal myelomeningocele or myeloschisis. All foetuses showed a second-degree Arnold–Chiari malformation with significant herniation of cerebellar structures. The surgical procedures were performed between 24<sup>+1</sup> and 26<sup>+0</sup> weeks gestational age, with estimated foetal weights from 524 to 810 g. The duration of surgery was from 255 to 430 min, skin to skin. Table 3 shows relevant characteristics of these patients.

The first five patients did not receive any anxiolytic premedication with the intention of reducing the overall exposure of the foetus to sedatives. Following the standard operating procedure of the Texas Children's Hospital in Houston, USA, the first four patients had general anaesthesia induced in the operating theatre after being placed in position for surgery, the skin prepped and sterile drapes applied. However, in our patients, this resulted in marked maternal anxiety and an urgent need for sedation with midazolam and/or propofol to control maternal blood pressure and heart rate until our team was able to start with the induction of anaesthesia. Beginning with the fifth patient, we induced anaesthesia in our induction room after placement of the epidural catheter. We choose to opt for this procedure, accepting that given the overall duration of the procedure and the concentrations of sevoflurane used, an additional 20 to 30 min under general anaesthesia was unlikely to affect outcomes. From patient 6 onwards, all mothers received 7.5 mg of oral midazolam 30 min before transfer to the induction room, which led to reduced maternal stress responses.

For fluid management, Ringer's acetate and albumin 5% were used. The overall volume of crystalloid fluids given was restricted drastically after patient 4 developed severe postoperative pulmonary oedema with high oxygen demand and a need for diuretic therapy. The overall amount of albumin 5% solution given was limited to approximately 10 ml kg<sup>-1</sup> and postoperative fluid intake was limited to 1500 ml per day (Table 3).

For the first four patients, the epidural analgesia with sufentanil 10 µg in 12 ml of ropivacaine 0.2% was started before incision. Beginning with patient 5, the initiation of the epidural was delayed until closure of the uterus: this helped with the maintenance of normotension during surgery.

For intra-operative analgesia, a remifentanil infusion at 0.1 to 0.3 µg kg<sup>-1</sup> min<sup>-1</sup> has been sufficient.

Most patients showed significant remaining neuromuscular block at the end of surgery and required reversal with neostigmine 1 to 3 mg and atropine 0.5 mg. All patients emerged from general anaesthesia without problems, and the trachea was extubated in the operating theatre. The patients were then transferred to an intermediate care unit where they were monitored for 48 h.

All except one patient gave birth at our hospital by both vaginal and caesarean delivery and as late as the 40th week of pregnancy (Table 3). There were no emergencies or severe complications regarding the foetuses or their mothers.

## Discussion

### Considerations for general anaesthesia during pregnancy

The procedure of spina bifida repair is usually performed at 19<sup>+0</sup> to 26<sup>+0</sup> weeks gestational age when many

**Table 3** The first 15 patients and relevant facts

Patient number	Mother Age (y)/ weight (kg)	Diagnosis	Gestation (weeks <sup>+</sup> days)	Foetal weight (g)	Duration of surgery (min)	Intravenous volume (ml) crystalloid/albumin	Foetal anaesthesia	Delivery/gestation
1	35/91	MMC L3-S1 + ACM2	25 <sup>+3</sup>	625	315	1500/450	4x	VD/36 <sup>+4</sup>
2	38/76	MMC L3-S1 + ACM2	26 <sup>+0</sup>	737	375	3000/750	5x	CD/38 <sup>+1</sup>
3	31/61	MMC L1-S3 + ACM2	25 <sup>+2</sup>	717	375	1000/1000	4x	CD/36 <sup>+5</sup>
4	37/75	Myeloschisis L4-L5 + ACM2	24 <sup>+6</sup>	682	375	1000/750	3x	VD/39 <sup>+1</sup>
5	31/71	Myeloschisis L3-S1 + ACM2	25 <sup>+2</sup>	729	285	250/750	3x	CD/38 <sup>+6</sup>
6	20/56	MMC Th12-S1 + ACM2	24 <sup>+4</sup>	610	370	250/750	4x	CD/37 <sup>+0</sup>
7	19/75	MMC L3-S3 + ACM2	25 <sup>+1</sup>	669	315	250/750	3x	CD/38 <sup>+1</sup>
8	27/68	MMC L5-S3 + ACM2	25 <sup>+2</sup>	723	255	250/500	3x	VD/34 <sup>+4</sup>
9	34/59	MMC L4-S2 + ACM2	25 <sup>+3</sup>	700	285	250/750	3x	Delivered elsewhere
10	30/89	MMC L3-S1 + ACM2	25 <sup>+5</sup>	670	430	200/750	5x	eCD/31 <sup>+2</sup>
11	30/83	MMC L4-S3 + ACM2	25 <sup>+3</sup>	730	340	250/800	3x	VD/37 <sup>+1</sup>
12	34/69	Myeloschisis L3-S3 + ACM2	24 <sup>+1</sup>	524	330	200/700	3x	CD/37 <sup>+2</sup>
13	31/85	Myeloschisis L5-S3 + ACM2	25 <sup>+1</sup>	747	380	300/750	3x	CD/36 <sup>+1</sup>
14	25/66	Myeloschisis L5-S4	24 <sup>+1</sup>	601	295	200/500	2x	VD/36 <sup>+5</sup>
15	32/120	MMC L5-S4	25 <sup>+4</sup>	810	326	350/1000	3x	VD/38 <sup>+4</sup>

ACM2, Arnold–Chiari malformation 2; CD, caesarean delivery; eCD, emergency caesarean delivery; i.v., intravenous; L and S, the lumbar and sacral levels of the lesion; MMC, myelomeningocele; VD, vaginal delivery.

pregnancy-related changes in maternal physiology are already in effect.<sup>13</sup> A higher incidence of difficult airways, together with a 20% increase in oxygen consumption and a 20% decrease in functional residual capacity can make airway management challenging during pregnancy.<sup>14</sup>

Gastric emptying is not delayed in comparison with nonpregnant women until the onset of labour. However, because of the elevated intra-abdominal pressure and a reduced oesophageal sphincter tone, the risk of aspiration is increased and measures such as RSI are recommended.<sup>14,15</sup> Alternatively point-of-care gastric ultrasound could be performed before induction of anaesthesia to help guide the decision whether RSI is necessary. This, however, is not yet an established practice in our institution.<sup>16</sup> Other physiological changes include a higher minute-ventilation with CO<sub>2</sub> partial pressures maintained at 27 to 34 mmHg, increased plasma volume leading to a lower haematocrit and lower serum albumin concentration due to dilution, increased cardiac output as well as the risk of inferior vena cava compression.<sup>13,17,18</sup>

To prevent foetal acidosis during CO<sub>2</sub> pneumotrium or pneumoperitoneum (if a laparoscopic approach is used), it is important to maintain normal CO<sub>2</sub> partial pressures for a pregnant patient (27 to 34 mmHg). This approach has been shown to be well tolerated in animal studies and in humans. So far, all foetuses have shown stable heart rates during general anaesthesia.<sup>19</sup>

To reduce the exposure of the foetus to anaesthetic medications, a point can be made for inducing anaesthesia after positioning, and sterile preparations are finished and the surgeons are ready for the skin incision, as is commonly practiced for caesarean deliveries. However, this approach leaves many patients extremely anxious and stressed during the preparations leading to tachycardia and hypertension and the need for sedation to control

these before the surgeons are ready for us to induce general anaesthesia. We argue that this is not in the best interest of our patient or the foetus, and may even cause harm because excessive stress can lead to uterine contractions or even labour.

Changes in maternal haemodynamics caused by anaesthetic drugs, positive-pressure ventilation and surgical stimuli must be anticipated. For haemodynamic support, it may be necessary to use vasopressors to keep maternal blood pressures within normal limits. In Germany, cafedrine/theodrenaline is often chosen as a vasopressor, internationally phenylephrine or norepinephrine are commonly used.<sup>13</sup>

At our institution, we use a combination of atosiban, magnesium sulphate and sevoflurane to ensure adequate uterine relaxation. The magnesium infusion is stopped before emergence and magnesium levels are measured after surgery. The need for magnesium sulphate is still under discussion as its disadvantages to the mother need to be weighed against benefits for the foetus. For the mother, there is long lasting neuromuscular block for several hours after an intubating dose of rocuronium while sugammadex should be avoided (it binds progesterone and data on the safety of the drug during pregnancy is inconclusive). In addition, even without neuromuscular block, magnesium sulphate induces significant muscle weakness. For the foetus, there is improved uterine relaxation and a degree of neuroprotection.<sup>20</sup>

One of the serious complications of foetal surgery is the risk of postoperative maternal pulmonary oedema. This is thought to be as a result of the lower serum osmolality during pregnancy, combined with the administration of tocolytics such as atosiban, magnesium or nitroglycerine, all of which can increase capillary leakage. The consequences of pulmonary oedema may be a need for ICU admission, diuretic therapy, or even intubation with prolonged ventilatory support.



Details on the incidence of pulmonary oedema after intrauterine foetal surgery are limited. However, one study of 187 mothers in a specialised foetal surgery centre who had undergone different foetal surgery procedures noted pulmonary oedema in 21.9% of the mothers.<sup>21</sup>

With the aim of reducing the incidence of pulmonary oedema, it is common to limit the volume of intravenous fluids given during surgery to less than 1 to 2 l. Our patients receive a maximum of 500 ml of Ringer's acetate and 10 ml kg<sup>-1</sup> of albumin 5%: this has led to good outcomes in our limited experience. However, there is currently no evidence as to whether restrictive fluid therapy improves outcomes in comparison with either a goal-directed fluid therapy using pulse contour analysis or a liberal fluid regimen.<sup>13</sup>

### Foetal physiology and considerations for anaesthesia

The most important parameter determining foetal cardiac output is the FHR. In comparison with the heart of an adult, the foetal heart is less contractile and can only increase its output by an increase in heart rate. A decrease in FHR and bradycardia (<100 beats min<sup>-1</sup>) is a sign of distress and must lead to timely corrective measures. Bradycardia can be caused by various stressors such as hypoxia, hypothermia or other noxious stimuli like pain. Foetal bradycardia can further lead to foetal acidosis, which also has negative effects on the haemodynamic of the foetus leading to a vicious cycle.<sup>18</sup>

Because the uterus is lacking in autoregulation for local perfusion pressures, the utero-placental blood flow and subsequently the oxygenation of the foetal blood is directly affected by maternal cardiac output as well as maternal oxygenation. Therefore, the maternal blood pressure should be maintained close to baseline values during anaesthesia, and adequate oxygenation must be ensured at all times.<sup>18,22</sup>

Hypothermia can become a problem during surgery when the abdomen is open and the uterus is filled with CO<sub>2</sub>, potentially leading to foetal bradycardia. The foetus has no means of regulating its own temperature and is kept warm by the mother. Adequate maternal temperature control is essential during surgery and can be achieved using warm blankets, forced air systems, a heated mattress, warmed intravenous fluids, heated CO<sub>2</sub> for uterine insufflation, and covering up the uterus as well as keeping the operating theatre temperature at higher levels.<sup>18,22,23</sup>

Foetal bradycardia should be treated immediately to prevent further haemodynamic compromise. Potential factors to be considered may include correcting maternal blood pressure, heart rate, oxygenation, and body temperature as well as the administration of tocolytics to stop uterine contractions. The surgical team may initiate leftward displacement of the uterus in the event of vena caval compression, repositioning of the foetus in the case

of kinking or compression of the umbilical cord, and intra-uterine infusion of warm fluids in the case of foetal hypothermia.

Severe foetal bradycardia (HR <100 min<sup>-1</sup>) not responding to the measures mentioned, should be treated with atropine and epinephrine intramuscularly to the foetus. Hysterotomy and cardiopulmonary resuscitation as well as emergency caesarean delivery may be necessary. A neonatology team should be available in case of emergency delivery. The possible need for foetal resuscitation should be discussed with the entire team before surgery and critical decision points such as foetal heart rates and the required resuscitative measures should be established.<sup>18</sup>

Certain medications given to the mother for general anaesthesia readily cross the utero-placental barrier and can directly affect the foetus. Although this may be desirable to facilitate foetal anaesthesia and analgesia, there are known negative effects. In addition to potential neurotoxic effects on the developing foetal brain, volatile anaesthetics such as sevoflurane or desflurane may reduce cardiac contractility and cause ventricular dysfunction as their concentrations within the foetus gradually increase during prolonged maternal administration.<sup>24</sup> This becomes important during fetoscopic SBA surgery as high doses of volatile anaesthetics are administered during phases of uterine manipulation. Some centres have tried using supplemental intravenous anaesthesia (SIVA), and administering propofol seems to reduce the need for large doses of volatile anaesthetics to provide adequate uterine relaxation and this might reduce foetal cardiac dysfunction.<sup>25</sup>

The question as to whether a foetus at a gestational age of 25 weeks can feel pain is controversial. In a review by Lee *et al.*, the authors argue that it is unlikely that a foetus can be aware of pain before the third trimester as the corresponding thalamocortical connections only start to function at 29 to 30 weeks of gestational age.<sup>26</sup>

However, painful stimuli can cause reflex movements of the foetus and trigger a hormonal stress response with the release of catecholamines and cortisol leading to decreased umbilical placental blood flow to/from the placenta. In addition, the endocrine response to pain can affect the uterus directly and cause premature labour.<sup>18,22</sup>

Although, volatile anaesthetics as well as opioids will readily cross the placenta, this is unlikely to provide sufficiently high concentrations in the foetal blood to prevent a foetal stress response in this type of surgery. Therefore, it is common practice in maternal-foetal surgery to administer opioids directly to the foetus via intramuscular injection.<sup>27,28</sup> Adding a paralytic to the foetal medications is associated with reduced complications and reduced foetal stress associated with the procedure.<sup>29</sup> Atropine may be added to prevent opioid-induced bradycardia.

These medications must be drawn up in a sterile fashion and prepared on a sterile field. This is done by the anaesthesiologist and an anaesthesia nurse in a distraction-free environment. The dosages should be based on the current estimated foetal weight provided by the obstetrics surgeons and should be cross-checked within the team to avoid mistakes. The team should also use some kind of sterile labelling system to prevent medication errors.

## Conclusion

Fetoscopic spina bifida repair surgery is a complex procedure, which requires a team effort to implement effectively. General anaesthesia during pregnancy and for foetal surgery is highly specialised and is not part of the day-to-day practice of most anaesthesiologists.

We have successfully implemented a standard operating procedure and have treated 15 patients as described above. Throughout the process, we have encountered complications such as pulmonary oedema and have adapted our approach to peri-operative fluid therapy. In future, the technique will undoubtedly undergo further changes as our team gains more experience or we become aware of new evidence.

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