

Anesthesia management for open fetal intrauterine surgery

J. Liu, Y. Ye, Z. Dong, Y. Liu, R. Ni, L. Zheng

Department of Anesthesiology, Foshan Children and Maternal Hospital, Foshan, Guangdong Province (China)

Summary

Objective: Open fetal surgery is usually performed during the second trimester in a fetus suffering from severe congenital diseases, thus enabling the pregnancy to continue until delivery. **Materials and Methods:** The key of this treatment is to promote uterine relaxation enough to maintain both maternal and fetal circulation stable and once surgery is completed, to offer a perfect analgesic to avoid the contractions due to pain, and finally to reduce preterm delivery. **Results:** Successful anesthesia is fundamental to this surgery. **Conclusion:** The authors have performed three cases under inhalation anesthesia combined with successful epidural anesthesia.

Key words: Open fetal surgery; Inhalation anesthesia; Epidural anesthesia; Analgesic.

Introduction

Nowadays, prenatal diagnosis allows people to better understand fetal intrauterine lesions. Successive prenatal ultrasounds have already been able to offer assistance in determining the natural pathological processes of fetal chest lesions and their pathophysiological characteristics affecting prognosis, based on which prognostic management protocols can then be proposed [1-6]. Successive prenatal ultrasounds have found that large fetal tumors can decrease in size, indicating that some fetal lesions have a self-improvement potential [7-9]. Ex utero intrapartum treatment (EXIT) can improve intrauterine lesions diagnosed late in pregnancy [10]. Open fetal surgery is also an important treatment procedure and can be applied in the treatment of predictable congenital diseases which affect fetal growth and development or even pose life-threatening consequences to the fetus, such as congenital diaphragmatic hernia, congenital high airway obstruction caused by endogenous laryngeal and tracheal deformities, exogenous airway compression, transoral tracheal intubation obstruction, severe dropsy caused by pulmonary congenital cystadenoma, bilateral tension pleural effusion, congenital chylothorax, unilateral pulmonary hypoplasia, congenital diaphragmatic hernia complicated by congenital heart disease, and so on [11-13].

Fetal surgery is a new treatment method appearing in recent years, which is based on the concept of "the fetus as a patient". Open fetal intrauterine surgery is among these. This procedure is often used to exert surgical treatment in a fetus at mid-trimester gestation complicated by severe congenital disease, and uterus suturing is then performed for the mother's on-going pregnancy until childbirth. However, this surgical procedure can lead to a relatively high incidence of postoperative complications. Furthermore, its required anesthesia management is also complex, in which attention must be simultaneously paid to both mother and fetus. The fetus must enter into a controlled anesthetized depth simultaneously with the

mother by maintaining intraoperative blood and oxygen supplies through the umbilical cord to the fetus, adequate postoperative sedation and analgesia are required, and the uterine contractions caused by pain should also be reduced to a minimum or even avoided in order to reduce the risk of a premature birth.

In 2011, the authors successfully performed surgical deep inhalation anesthesia for three women during pregnancy, complicated by fetal pulmonary cystadenoma.

Materials and Methods

Three women in their child-bearing period were involved. Admitting diagnoses and B ultrasounds were performed in them.

Case 1

The woman had a history of two pregnancies and one delivery. The fetus was at 28 + three weeks gestation and in a right sacrotransverse position with left lower pulmonary cystadenoma. B ultrasound revealed that the fetus had a heart dextroposition but without structural anomalies in it and was in a breech position; there was no anomaly in the amniotic fluid volume; the placental maturity was 0 + degrees; and an approximate 5.6 × 5.0 × 5.0 cm hyperechoic mass in a triangle-like image was seen in the fetus' left thoracic cavity. The mass echoes were irregular and there were several tiny cystic dark regions; it was the cause of the fetal heart dextroposition.

Case 2

The woman had a history of one pregnancy but without a delivery. The fetus was at a 28 + five weeks gestation age and in a left occipital anterior position with a congenital cystadenoma-like deformity in the left lung. B ultrasound was performed. The fetus was in a cephalic position at a gestation age equivalent to 28 + weeks. No anomaly was detected in the amniotic fluid volume. The placenta was located at the right and posterior walls with a maturity degree of 0 +. An approximate 4.8 × 2.6 × 3.2 cm hyperechoic mass was detected in the fetus' left thoracic cavity, in which a few scattered dark areas could be seen, with the maximum one of approximately 0.2 × 0.2 cm in size. No independent blood flow from the aorta was detected. The fetus's heart was transpositioned into the right thoracic cavity due to the complete compression of the mass. Normal pulmonary tissue echoes were received from the

upper region of the left thoracic cavity with an area of approximately 1.3×1.2 cm. The size of the left mass under the four chambers was around 3.5×3.8 cm, while that of the right lung was around 3.0×1.5 cm. Neither subcutaneous edema nor noticeable splanchnocoel or pericardial effusion was detected in the fetus.

Case 3

The woman had a history of one pregnancy but without a delivery. The fetus was at 29 weeks gestation and in a right occipital transverse position with a congenital cystadenoma-like deformity in the left lung. B ultrasound showed that the fetus was at a gestation age equivalent to 28 + weeks, the amniotic fluid index was 28, and the placental maturity degree was 0 +; an approximate $7.1 \times 4.6 \times 5.6$ cm hyperechoic mass was seen in the fetus' left thoracic cavity, in which multiple liquid anechoic areas with varying sizes could be detected; the heart and mediastina were transpositioned into the right thoracic cavity under compression, and heart oscillation could be detected. The fetus was diagnosed with pulmonary cystadenoma.

Open fetal surgery (left pulmonary cystadenoma resection) under deep inhalation combined with epidural anesthesia was performed for the three pregnant women. All of them were in a physical status I-II, according to American Society of Anesthesiologists grading. They were free of endocrine system diseases and important organ diseases.

Anesthesia and surgery

Continuous epidural anesthesia and inhalation anesthesia were combined in the anesthesia management.

The women were abstained routinely from food and drink. Scopolamine (0.3 mg) was given intramuscularly 30 minutes before surgery. Two venous channels were opened for the connections to the anesthesia depth monitor. An epidural puncture was performed through the L2-3 interspace in a left-lateral position for intubation. When no blood or cerebrospinal fluid could be pumped back, two percent lidocaine at five ml as a test dose was infused. Intravenous anesthesia induction was instantly performed after a sensation block level turned up, using midazolam (0.1 mg/kg), propofol (1.5 mg/kg), fentanyl (three μ g/kg), and cisatracurium besylate (0.15 mg/kg). Endotracheal catheters with an inside diameter of seven mm were successfully inserted after mask oxygen inhalation, and auscultation showed that the bilateral pulmonary respiratory sounds were clear and balanced. The catheters were fixed, and respiration was controlled with a tidal volume at ten ml/kg, a respiratory frequency at 12 times/min, and an inspired oxygen concentration at 75%. In the meantime, the isoflurane concentration was adjusted to three percent with an oxygen flux at 31 min to increase the exhaled isoflurane concentration to less than two percent. A right subclavian vein puncture was performed to establish a central venous channel for central venous pressure (CVP) monitoring. A radial arterial puncture and intubation were performed for direct arterial pressure monitoring.

Fetal position and heart rate were preoperatively determined by B ultrasound. Dopamine was pumped intravenously for intraoperative adjustment, according to maternal blood pressure and heart rate. Sufentanil (0.2 μ g/kg), cisatracurium besylate (0.15 mg/kg), and 0.04% Anpo (15 drips/min) were added when the skin was cut. The fetal position and heart rate were determined again by B ultrasound before the uterus was opened. After uterine opening, one of the fetus' arms was connected to blood-oxygen saturation and rectal temperature probes and one fetal

peripheral venous channel was then opened. Anpo (a uterine contraction inhibitor) was adjusted to 25 drips/min. The fetal operative field was exposed. During operation, lactated Ringer's solution at 40°C as amniotic fluid was continuously infused for the maintenance of the fetal external environment, body temperature, and skin humidity while B ultrasound was used for fetal heart rate and heart status monitoring. Decreased heart rates were monitored in the two fetuses with larger cystic adenomatoid masses after tumor resection, with the minimum rate of 75 beats/min. The fetuses were injected intravenously with atropine and adrenaline and then supplemented with erythrocyte suspension. Their heart rates returned to more than 145 beats/min again after infusion. After fetal operation, the exposed limb was repositioned into the uterus. Then, the inhaled isoflurane concentration was reduced to maintain an exhaled concentration at 1.5%. Meanwhile, sufentanil (0.2 μ g/kg) was added intravenously for further maternal intervention. Isoflurane inhalation was stopped after the closure of the peritoneum. Postoperatively, the mother returned to spontaneous respiration and the endotracheal catheters were withdrawn under deep anesthesia. The mother was sent to the intensive care unit for 24 hours' observation and then returned to her regular room. The mean anesthesia and maternal and fetal surgical times were three hours and 20 minutes, two hours and 30 minutes, and 29 minutes, respectively. Intraoperative supplemented crystal solution was 2,150 ml. The fetal hemorrhage volume was around four ml. The maternal hemorrhage and urinary volumes were around 50 ml and 300 ml, respectively.

Results

The women continuously received anti-infection and uterine contraction-inhibiting treatment after operation. They recovered well without obstetric complications. They presented premature ruptures of the membrane at gestational 32, 33, and 34 weeks and underwent cesarean sections, respectively. All the newborns were alive. They were ventilated mechanically after being delivered. However, the newborn of 33 weeks' gestation age died of pulmonary maldevelopment. The other two survived and recovered well.

Discussion

Anesthesia for the mother involved in fetal surgery has a much higher risk than that for common cesarean section. The induction and maintenance of general anesthesia will affect the physiological environments of the mother's important organs. Pregnancy changes the anatomical relations of the esophagus with the transeptae and stomach. This condition decreases the mother's functional residual capacity and gradually increases her oxygen consumption. Pregnancy also exerts influences on the cardiovascular and central nervous systems. Supine hypotension syndrome can lead to maternal hypotension, fetal anoxia, an obvious decrease in the minimum alveolar concentration, and an increase in susceptibility to muscle relaxants [14-18].

In open intrauterine surgery, it is crucial to maintain the uterus in a relaxed state at all times. Therefore, adequate analgesia, sedation, and muscle relaxation should

be ensured and uterine contraction inhibitors should be continuously applied during perioperation. Among different uterine contraction inhibitors, Anpo has been proved to have the most specific inhibitory effect and has been widely used clinically. However, Anpo can lead to an increase in maternal heart rate, which can further influence the fetus' heart rate. Therefore, a balance between sufficient uterine relaxation and maternal and fetal cardiovascular stabilities during open intrauterine surgery is necessary. However, heart rate control itself is a matter of medical debate. Some scholars believe that strict heart rate control is unnecessary because blood pressure can be adjusted through maternal heart rate changes to reduce the interventions from external drugs.

Fetal immature organ function renders anesthesia for the fetus rather difficult to perform. To perform it, reliable fetal monitoring is needed first, such as blood oxygen saturation and body temperature monitoring through the fetus' exposed limb, B ultrasound for the fetus' cardiac function, and so on. Maintaining fetal cardiovascular stability is the most important step in anesthesia management for fetal surgery. The fetus improves oxygenation by resorting to increases in cardiac output and blood flow redistribution, while the cardiac output depends on the fetus' heart rate. Under stress, the hyposensitivity of the highly-aberrant tension and pressure-receptive cells in the fetus always leads to a decrease in heart rate. In addition, since the circulating blood volume in a fetus is very small, even a small amount of blood loss in surgery may cause fetal hypovolemia [19]. Based on these reasons, after a large mass was removed from the lung, mediastinal swaying which led to arrhythmia and heart failure became unavoidable in the present study. Furthermore, inhalation anesthesia can cause direct inhibition of the fetal cardiac muscle, as well as vasodilatation, which may further lead to arteriovenous shunt, ultimately destroying the balance of the cardiovascular system [20]. The inhibitory effect of inhalation anesthesia on the fetal cardiac muscle can be aggravated with the prolongation of anesthesia time. Therefore, to ensure the life safety of the fetus is another key point in fetal intrauterine surgery.

Fetal survival depends on the mother, in which maternal blood pressure maintenance plays an important role. Normally, maternal blood pressure should be maintained within a range of ten percent based on the baseline. The blood flow velocity in the fetal aortic artery is influenced by fetal cardiac output and vascular resistance, so the maintenance of cardiac output plays a critical role in ensuring a sufficient oxygen supply to the fetus. Intraoperative control over the tension of the uterine smooth muscle can be fulfilled by using uterine contraction inhibitors and inhalation anesthetics. Compared with uterine contraction inhibitors, deep inhalation anesthesia can lead to uterine smooth muscle complete relaxation, which will be more convenient for surgery. Inhalation anesthesia however, has a drawback: it has an inhibitory effect on fetal cardiac vessels, which can lead to a reduc-

tion in uterine placental blood flow [20, 21]. Nevertheless, considering that almost all vasoactive drugs have a contractive effect on uterine placental vessels, deep inhalation anesthesia is still a better choice. In the future, however, a more rational application of vasoactive drugs in which the maternal blood circulation stability can be maintained on the one hand, and the influence of these drugs on the fetus can be reduced to the minimum on the other hand, remains to be explored.

In addition, postoperative analgesia for pregnant women also plays a crucial role. Thorough analgesia can reduce uterine contractions caused by pain, thus, to reduce the incidence of premature deliveries. In this study, uterine contractions caused by pain and preoccupation were basically eliminated in the three pregnant women. Fetal heart monitoring showed that the fetal heart sounds were slightly faster than normal, which is presumably correlated with the application of Anpo, and the intrauterine pressures were within the normal range.

In summary, the inhalation anesthetic isoflurane has a good effect in the anesthesia management for open fetal intrauterine surgery. However, what advantages and disadvantages does sevoflurane have as compared to isoflurane? Is it necessary to strictly control the maternal heart rate by using drugs during surgery? Can steroidal anti-inflammatory drugs be used for postoperative analgesia, and when can these drugs be used? These questions remain to be solved.

References

- [1] Adzick N.S., Harrison M.R., Glick P.L., Golbus M.S., Anderson R.L., Mahony B.S. *et al.*: "Fetal cystic adenomatoid malformation: prenatal diagnosis and natural history". *J. Pediatr. Surg.*, 1985, 20, 483.
- [2] Thorpe-Veeston J.G., Nicolaides K.H.: "Cystic adenomatoid malformation of the lung: prenatal diagnosis and outcome". *Prenat. Diagn.*, 1994, 14, 677.
- [3] Sakala E.P., Perrott W.S., Grube G.L.: "Sonographic characteristics of antenatally diagnosed extralobar pulmonary sequestration and congenital cystic adenomatoid malformation". *Obstet. Gynecol. Surv.*, 1994, 49, 647.
- [4] Miller J.A., Cortevill J.E., Langer J.C.: "Congenital cystic adenomatoid malformation in the fetus: natural history and predictors of outcome". *J. Pediatr. Surg.*, 1996, 31, 805.
- [5] Dimmergues M., Louis-Sylvestre C., Mandelbrot L., Aubry M.C., Révillon Y., Jarreau P.H. *et al.*: "Congenital adenomatoid malformation of the lung: when is active fetal therapy indicated?". *Am. J. Obstet. Gynecol.*, 1997, 177, 953.
- [6] Taguchi T., Suita S., Yamanouchi T., Nagano M., Satoh S., Koyanagi T. *et al.*: "Antenatal diagnosis and surgical management of congenital cystic adenomatoid malformation of the lung". *Fetal. Diagn. Ther.*, 1995, 10, 400.
- [7] Saltzman D.H., Adzick N.D., Benacerraf B.R.: "Fetal cystic adenomatoid malformation of the lung: apparent improvement in utero". *Obstet. Gynecol.*, 1988, 71, 1000.
- [8] MacGillivray T.E., Harrison M.R., Goldstein R.B., Adzick N.S.: "Disappearing fetal lung lesions". *J. Pediatr. Surg.*, 1993, 28, 1321.
- [9] Laberge J.M., Flageole H., Pugash D., Khalife S., Blair G., Filiatrault D. *et al.*: "Outcome of the prenatally diagnosed congenital cystic adenomatoid lung malformation: a Canadian experience". *Fetal. Diagn. Ther.*, 2001, 16, 178.
- [10] Hedrick H.L., Flake A.W., Crombleholme T.M., Howell L.J., Johnson M.P., Wilson R.D. *et al.*: "The ex utero intrapartum therapy procedure for high-risk fetal lung lesions". *J. Pediatr. Surg.*, 2005, 40, 1038.

- [11] Eschertzhuber S., Keller C., Mitterschiffthaler G., Jochberger S., Kühbacher G.: "Verifying correct endotracheal intubation by measurement of end-tidal carbon dioxide during an ex utero intrapartum treatment procedure". *Anesth. Analg.*, 2005, 101, 658.
- [12] Preciado D.A., Rutter M.J., Greenberg J.M., Bahado-Singh R., Lambers D., Willging J.P.: "Intrapartum management of severe fetal airway obstruction". *J. Otolaryngol.*, 2004, 33, 283.
- [13] Ogamo M., Sugiyama T., Maeda Y., Kusaka H., Utsunomiya H., Tsubouchi M. *et al.*: "The ex utero intrapartum treatment (EXIT) procedure in giant fetal neck masses". *Fetal Diagn. Ther.*, 2005, 20, 214.
- [14] Strout C.D., Nahrwoldm M.L.: "Halothane requirement during pregnancy and lactation in rats". *Anesthesiology*, 1981, 55, 322.
- [15] Gin T., Chan M.T.: "Decreased minimum alveolar concentration of isoflurane in pregnant humans". *Anesthesiology*, 1994, 81, 829.
- [16] Chan M.T., Gin T.: "Postpartum changes in the minimum alveolar concentration of isoflurane". *Anesthesiology*, 1995, 82, 1360.
- [17] Palahniuk R.J., Shnider S.M., Eger E.I.: "Pregnancy decreases the requirement for inhaled anesthetic agents". *Anesthesiology*, 1974, 41, 82.
- [18] Chan M.T., Mainland P., Gin T.: "Minimum alveolar concentration of halothane and enflurane aer decreased in early pregnancy". *Anesthesiology*, 1996, 85, 782.
- [19] MacGregor S.N., Socol M.L., Pieler B.W., Sholl J.T., Minogue J.P.: "Prediction of fetoplacental blood volume in isoimmunized pregnancy". *Am. J. Obstet. Gynecol.*, 1988, 159, 1493.
- [20] Palahniuk R.J., Shnider S.M.: "Maternal and fetal cardiovascular and acid-base changes during halothane and iosflurane anesthesia in the pregnant ewe". *Anesthesiology*, 1974, 41, 462.
- [21] Gaiser R.R., Kurth C.D., Cohen D., Crombleholme T.: "The cesarean delivery of a twin gestation under 2 minimum alveolar anesthetic concentration isoflurane: one normal and one with a large neck mass". *Anesth. Analg.*, 1999, 88, 584.

Address reprint requests to:
 J. LIU, M.D.
 Department of Anesthesiology
 Foshan Children and Maternal Hospital
 No. 11 Renmin Road, Chancheng District
 Foshan 528000 (China)
 e-mail: jipingliu@126.com