THE JOURNAL OF
Obstetrics and Gynaecology Research

doi:10.1111/jog.13895 J. Obstet. Gynaecol. Res. Vol. 45, No. 3: 719–723, March 2019

Long tail balloon as a new approach for fetoscopic tracheal occlusion for a treatment of severe congenital diaphragmatic hernia

Michael Tchirikov[1], Carsten Springer[2], Sven Seeger[3], Curd Behrmann[4], Michael Bergner[1] and Roland Haase[5]

University Clinic [1]of Obstetrics and Prenatal Medicine, [4]of Radiology, [5]of Pediatrics, Martin Luther University Halle-Wittenberg, [3]Department of Obstetrics, St. Elisabeth Hospital, Halle and [2]Department of Obstetrics, St. Elisabeth Hospital, Leipzig, Germany

Abstract

Severe congenital diaphragmatic hernia (CDH) remains a significant challenge for neonatal specialists. In order to reduce complications during extraction of the surgical balloon after fetoscopic tracheal occlusion (FETO) CDH, we have developed a FETO with a 'long tail balloon' of 2.5 mL volume. Here we describe two successful uses of the device with observed/expected total fetal lung volume (o/e TFLV) of 15% and with o/e TFLV of 24% and 'liver up'. The o/e TFLV increased to 134% in first case and to 47% in second fetus. The balloon was successfully extracted at 34 weeks' gestation by pulling the long tail suture during second fetoscopy. In the second case the fetus pulled out the balloon from trachea itself by traction onto the balloon's long tail. Both neonates were operated on for their CDH with a good outcome. This work showed the feasibility of this long tail balloon for FETO to reduce the technical difficulty of the balloon extraction and the possibility that fetuses are able to extract the balloon by itself by pulling the balloons' long tail. Further development of long tail balloon for FETO could facilitate its extraction thereby reducing neonatal complications.

Key words: balloon extraction, CDH, congenital diaphragmatic hernia, fetoscopic tracheal occlusion, fetoscopy, long tail balloon.

Introduction

Congenital diaphragmatic hernia (CDH) has an incidence of 1:2200 to 1:4000 newborns, depending on whether stillbirths are included or not.[1,2] Forty percent of all CDH cases show associated malformations and chromosomal abnormalities with recognized syndromes occurring in 10–20%.[1–3] Importantly, the survival depends on the extent of the lung hypoplasia and pulmonary hypertension.[4] Liver herniation into the thorax, is also a negative predictor of fetal survival. In case of an observed or expected total fetal lung volume ratio (o/e TFLV) ratio of 25% or lower, and herniation of the liver in thorax, the postnatal survival is reported to be 10–25% or lower.[5–7] The aim of fetoscopic tracheal balloon occlusion is to positively influence the lung growth in CDH fetuses, avoiding the development of lung hypoplasia.[5,8] As the lung fluid cannot pass though the latex balloon in the trachea, and so leads to an expansion of the lungs.

A common complication of fetal surgery is the preterm premature rupture of membranes (PPROM) leading to preterm delivery.[1,5,9] The next problem faced by clinicians, is the technical difficulties of the extraction of the balloon from the trachea, possibly leading to asphyxia, worse outcome or neonatal

Received: February 27 2018.
Accepted: November 30 2018.
Correspondence: Prof. Dr. Michael Tchirikov, University Clinic of Obstetrics and Prenatal Medicine, Center of Fetal Surgery, University Hospital Halle (Saale), Martin Luther University Halle-Wittenberg, Ernst-Grube Strasse 40, 06120 Halle (Saale), Germany.
Email: michael.tchirikov@uk-halle.de

demise.[5] Jani *et al*.[5] published 10 neonatal deaths from 210 fetoscopic tracheal occlusion (FETO) performed, directly related to difficulties with the removal of the intratracheal balloon. The risk of emergency balloon removal is published to be very high (39–56%).[5,10]

This work showed the feasibility of this long tail balloon for FETO to reduce the technical difficulty of the balloon extraction and the possibility that fetuses are able to extract the balloon by itself by pulling the balloons' long tail.

Case Report

Case 1

A 35–year-old woman, gravida 1 pare 0 was referred to our center of fetal surgery at 24^{+1} weeks' gestation because of severe CDH with o/e TFLV of 15%.[7]

The FETO was performed with the permission of local ethic committee for individual treatment and written patients' consent. The tracheal occlusion (TO) was performed at 28^{+4} weeks' gestation. The fetus received i.m. 0.1 mg/kg Pancuronium, 1 μg/kg Fentanyl and 0.01 mg/kg atropine.

The monofilament 5-0 polypropylene suture of 7 cm was fixed to the balloon (Goldbal 5, 2.5 mL, BALT Extrusion, Montmorency, France) (Fig. 1). The fetoscope (Karl Storz, Tuttlingen, Germany) with a diameter of 1.3 mm, was percutaneously inserted through a sheath into the uterus and then into the fetal trachea. The fetoscope was removed and the balloon was inserted through the sheath into the trachea under 4-D ultrasound guidance.[11,12]

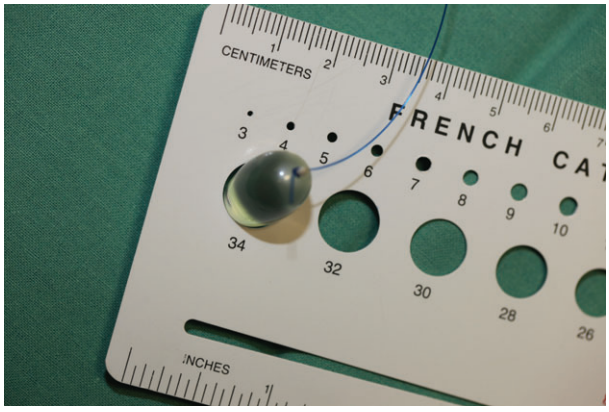

Figure 1 Long tail tracheal balloon. The monofil polypropylen 7 cm suture fixed to the balloon (Goldbal 5, 2.5 mL, BALT Extrusion, Montmorency, France) before the fetoscopic intratracheal occlusion.

The position of the balloon and suture were visualized by ultrasound and magnetic resonance imaging (MRI) (Fig. 2). Two months after FETO the MRI estimated the o/e TFLV ratio to be increased from 15 to 134%. We decided to remove the intratracheal balloon by fetoscopy. The balloon was extracted by traction and suture rolling over the fetoscopic miniature forceps. The patient was delivered at 37^{+1} weeks' gestation by planned primary C-section), a girl, weighing 2540 g, length 50 cm, APGAR 4/8/9, umbilical artery pH 7.28. One week after the CDH operation the girl was extubated. Additionally, final diagnoses confirmed a polycystic left kidney, anal atresia with fistula and polydactyly of the right hand. One month later the baby was discharged from hospital in good condition. In follow up examinations at 6 months and 1 year of age, the baby was doing well without any neurological disturbance or developmental delay.

Case 2

A 29-year-old, first gravida woman was referred to the university clinic with severe CDH at 29 weeks' gestation. The MRI measured o/e TFLV ratio was 24.6%. The FETO with modified 'long tail' balloon was performed at 29^{+5} weeks. The video documentation of the fetoscopic procedure and correct intratracheal location of the balloon was performed. The o/e TFLV ratio increased to 47% after the FETO procedure. The patient was delivered by c-section because of PPROM at 34^{+4} weeks of gestation and intubated, a boy weighing 2250 g, APGAR 6/7/8, umbilical artery pH 7.35. After the intubation the balloon was found to be swallowed in neonatal esophagus. Using endoscopic examination it was extracted by the neonatal team. The CDH was closed with a patch and the pulmonic sequester was resected. In follow up examinations at 6 months of age the baby was breast feeding without any neurological disturbances or developmental delay apparent.

Discussion

In this report we have described a new approach for FETO procedure for CDH treatment.

The CDH affects approximately one of every 2200–4000 live births.[1–3] Approximately 60% of CDH cases are isolated.[2] In about 10–20% of cases of CDH diagnosed prenatally, there are also chromosomal abnormalities, such as trisomies 13, 18 and 21, or Fryns, Beckwith-Wiedermann, Pierre-Robin, Pallister-

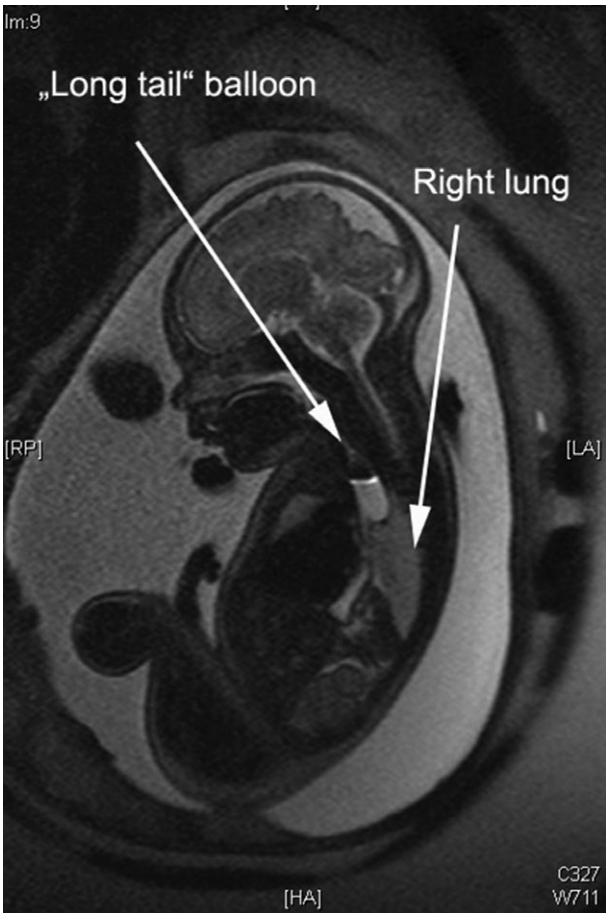

Figure 2 Fetal magnetic resonance imaging (MRI) after the fetoscopic tracheal occlusion using long tail balloon. The fetus is present in sagittal position. The balloon can be clearly identified in the fetal trachea. The volume of the right lung was normalized after 4 weeks in response to the tracheal occlusion.

Killian syndromes.[1,2] The clinical course of fetuses with isolated CDH depends entirely on the degree of pulmonary hypoplasia and severity of pulmonary hypertension.[2] Isolated small diaphragmatic defects do not normally lead to pulmonary hypoplasia and can be successful corrected after the delivery.[4] Intrauterine fetal tracheal balloon occlusion is the most common prenatal therapy for fetuses with large CDH and a very poor prognosis.[1,5,8,13] The herniation of the liver into the thorax is an independent negative prediction value for postnatal survival.[1,2,4,5] Compared to conservative management of fetuses with severe CDH, fetuses with left CDH treated with FETO had an increased survival rate, from 24 to 49%, and in right CDH from 0 to 35.3%.[5] Ali *et al*. also published the similar survival rate of 48%. Ruano *et al*. published the fetal survival after early FETO of 62.5%.[10,14]

A major consideration is that the tracheal balloon needs to be removed before delivery in fetal treatment centers with a permanent experienced team, knowledgeable in all possible techniques. Jani *et al*.[5] published 10 neonatal deaths directly related to difficulties with removal of the intratracheal balloon. Wegrzyn *et al*.[15] also reported two neonatal deaths because of problems with balloon removal after the delivery. A second fetoscopic surgery to remove the balloon is usually planned at 34 weeks. It is also associated with increased risks for perioperative complications, PPROM, preliminary delivery and rarely uterine bleeding or injury of the fetus or mother.[1,5,6,13,14] Leading medical centers with most experiences of FETO show a high rate of PPROM after intrauterine fetal surgery using a 3 mm sheath.[5,10,15] Ali *et al*.[10] registered the premature delivery after FETO in 84%. Out of 24 infants, 23 who had emergency balloon removal were born before 35 weeks gestation.[10] Jani *et al*.[5] found the rate of PPROM after FETO to be 47.1%. The risk of PPROM after fetoscopy could be reduced by the reduction of the damage of the amniotic membranes using ultra-thin fetoscopic equipment combined with the 4-D ultrasound control.[9,11,12] An imminent delivery before the removal of the balloon is a life threatening situation for the unborn baby since the re-establishment of the airways represents a challenge even for experienced physicians.[5,6] In this scenario, the delivery is usually performed by ex utero intrapartum treatment (EXIT)-procedure, which is associated with severe risks, again even if performed in a specialist care center.[5]

The timing of the balloon removal must be planned and controlled and the risks of its use need to be considered and managed. Cannie *et al*. found in 2 of 31 cases the balloon deflation had low liver-to-thoracic volume ratio. Jani *et al*.[5] reported that in 8% of all cases after FETO there was spontaneous deflation and subsequent expulsion of the balloon. We described previously the method with insertion of the bigger latex balloon with the volume of 2.5 mL instead of conventional 0.75 mL balloon to guarantee better sealing of the trachea without leak of lung fluid.[11,12] Additionally, the TO before birth could decrease the number of pneumocytes type II in the alveoli.[16] .

The fetal ability to remove intrauterine implanted supravesical or thoracic shunts is well-known. We observed many times the ‘successful’ extraction of the

'pig tail' catheters placed intrauterine into the fetal bladder because of low urethral tract obstruction with an oligohydramnios by the fetuses themselves. The intensive fetal movements, swallowing reflex and also hand grasping are well documented during ultrasound examination and fetal surgery. This fetal grasping activity could be used for the programmed dislodgment of tracheal balloon due to fetal grasping traction to balloons' 'long tail'. In our second patient, the fetus probable was able to remove the tracheal balloon before the delivery. Unfortunately, the fetus could not take the balloon out into the amniotic cavity, but swallow into the esophagus possibly by the fetal swallowing reflex.

It is quite obvious that the latex balloon was extracted by the fetus from the trachea immediately stimulated the fetal swallowing reflex. For this reason, the tracheal balloons' 'long tail' must be connected to the valve or must have the valve construction inside of the 'long tail' for the controlled deflation of the balloon by the fetus itself. We assume that the minimal force of the valve must be about 0.5–1 N. However, this must be proved and optimized experimentally, probably in non-human primates, in order to avoid the extraction of the tracheal balloon before the lungs of CDH fetus reacts with adequate increased total lung volume to the TO.

Using the suture fixation to the balloon described above, the extraction of balloon was very simple during fetoscopy in the first patient. The use of long tail balloon could also facilitate the removal of the balloon from the trachea after emergency delivery or during the EXIT procedure. We have not observed any damage of fetal lips due to polypropylene suture to date. However, the creation of a new 'long-tail' is important to avoid any possible complications. We have not observed any signs of tracheomalcia in our CDH patients. However, the risk of this complication is expected to be higher compared to the use of the smaller latex balloon.[10] Ali *et al*.[10] described two cases having tracheomalacia using for the 61 CDH patients a latex balloon with the volume 0.75 mL.

Here, we describe a new approach for FETO procedure for CDH treatment, which might simplify the removal of the intratracheal placed balloon after emergency delivery, EXIT procedure, during the second fetoscopy or by the fetus itself at the end of the pregnancy. Our initial aim to develop the long-tail balloon modification was to reduce the risk of emergency balloon removal. The unexpected finding was the balloon removal by probably the fetus itself in the second case.

The concept of long tail balloon construction must be optimized and evaluated in prospective studies. The prospective study 'FETO with Long Tail Balloon for a Treatment of Severe CDH' has been started in our center of fetal surgery (NCT03431792, ClinicalTrials.gov).

Disclosure

The authors report no conflicts of interest.

The investigators do not have any financial relationship with companies.

'Long Tail Balloon' has been submitted for the patent application by the University Medical Center of the Martin-Luther-University Halle-Wittenberg, Germany.

References

1. Entezami M, Lebek H, Albig M, Hagen A, Tchirikov M. Pränatale Diagnostik der Zwerchfellhernie. *Gynäkol. Prax* 2012; **36**: 241–250.
2. Bianchi DW. *Fetology: Diagnosis and Management of the Fetal Patient*, 2nd edn. New York, NY: McGraw-Hill Medical, 2010.
3. Rottier R, Tibboel D. Fetal lung and diaphragm development in congenital diaphragmatic hernia. *Semin Perinatol* 2005; **29**: 86–93.
4. Oluyomi-Obi T, Kuret V, Puligandla P *et al*. Antenatal predictors of outcome in prenatally diagnosed congenital diaphragmatic hernia (CDH). *J Pediatr Surg*; 2017; **52**: 881–888. https://doi.org/10.1016/j.jpedsurg.2016.12.008.
5. Jani JC, Nicolaides KH, Gratacos E *et al*. Severe diaphragmatic hernia treated by fetal endoscopic tracheal occlusion. *Ultrasound Obstet Gynecol* 2009; **34**: 304–310. https://doi.org/10.1002/uog.6450.
6. Jani JC, Benachi A, Nicolaides KH *et al*.; Antenatal-CDH-Registry Group. Prenatal prediction of neonatal morbidity in survivors with congenital diaphragmatic hernia: A multicenter study. *Ultrasound Obstet Gynecol* 2009; **33**: 64–69. https://doi.org/10.1002/uog.6141.
7. Cannie M, Jani J, Meersschaert J *et al*. Prenatal prediction of survival in isolated diaphragmatic hernia using observed to expected total fetal lung volume determined by magnetic resonance imaging based on either gestational age or fetal body volume. *Ultrasound Obstet Gynecol* 2008; **32**: 633–639. https://doi.org/10.1002/uog.6139.
8. Al-Maary J, Eastwood MP, Russo FM, Deprest JA, Keijzer R. Fetal tracheal occlusion for severe pulmonary hypoplasia in isolated congenital diaphragmatic hernia: A systematic review and meta-analysis of survival. *Ann Surg* 2016; **264**: 929–933. https://doi.org/10.1097/SLA.0000000000001675.
9. Tchirikov M, Oshovskyy V, Steetskamp J, Falkert A, Huber G, Entezami M. Neonatal outcome using ultrathin fetoscope for laser coagulation in twin-to-twin-transfusion

syndrome. *J Perinat Med* 2011; **39**: 725–730. https://doi.org/10.1515/JPM.2011.091.
10. Ali K, Grigoratos D, Cornelius V, Davenport M, Nicolaides K, Greenough A. Outcome of CDH infants following fetoscopic tracheal occlusion – Influence of premature delivery. *J Pediatr Surg* 2013; **48**: 1831–1836. https://doi.org/10.1016/j.jpedsurg.2013.01.049.
11. Tchirikov M. Successful tracheal occlusion using ultrathin fetoscopic equipment combined with real-time three-dimensional ultrasound. *Eur Surg Res* 2009; **43**: 204–207. https://doi.org/10.1159/000224146.
12. Tchirikov M, Gatopoulos G, Strohner M, Puhl A, Steetskamp J. Two new approaches in intrauterine tracheal occlusion using an ultrathin fetoscope. *Laryngoscope* 2010; **120**: 394–398. https://doi.org/10.1002/lary.20687.
13. Ruano R, Yoshisaki CT, da Silva MM *et al*. A randomized controlled trial of fetal endoscopic tracheal occlusion versus postnatal management of severe isolated congenital diaphragmatic hernia. *Ultrasound Obstet Gynecol* 2012; **39**: 20–27. https://doi.org/10.1002/uog.10142.
14. Ruano R, Peiro JL, da Silva MM *et al*. Early fetoscopic tracheal occlusion for extremely severe pulmonary hypoplasia in isolated congenital diaphragmatic hernia: Preliminary results. *Ultrasound Obstet Gynecol* 2013; **42**: 70–76. https://doi.org/10.1002/uog.12414.
15. Wegrzyn P, Weigl W, Szymusik I *et al*. Premature labor after fetal endoscopic tracheal occlusion for congenital diaphragmatic hernia: Post-procedure management problems. *Ultrasound Obstet Gynecol* 2010; **36**: 124–125. https://doi.org/10.1002/uog.7697.
16. Flageole H, Evrard VA, Piedboeuf B, Laberge JM, Lerut TE, Deprest JA. The plug-unplug sequence: An important step to achieve type II pneumocyte maturation in the fetal lamb model. *J Pediatr Surg* 1998; **33**: 299–303.