

Antenatal Diagnosis & EXIT (Ex-Utero Intrapartum Treatment) Procedures

Gavin Morrison and José Nélio Cavinatto

Introduction

José Nélio Cavinatto

Congenital abnormalities in the head and neck may cause airway obstruction in the newborn, requiring immediate intervention. In the past, many newborns succumbed to airway obstruction because of the inability to establish a safe airway at delivery. Technological advances in prenatal ultrasonography and MRI have improved the ability to diagnose congenital abnormalities in utero. This allows for proper assessment of the airway to prevent any unexpected problems at delivery. We believe that many of the airway emergencies can be avoided by prenatal imaging and initiation of airway management in the prenatal period.

Fetal surgery and the ex utero intrapartum treatment (EXIT) procedure are used to manage these complex cases. These procedures were designed to provide time to secure an airway while uteroplacental gas exchange is preserved. In this study, is being described the King's College Hospital experience with the diagnosis and management of fetal cervical neck masses and discussed the efficacy of prenatal imaging and the safety of the EXIT procedure in these patients.

Gavin Morrison

This is a rare topic. The work I am going to discuss on foetal surgery takes place at the King's College Hospital, in South London, United Kingdom (UK).

Increasing sophistication of antenatal ultrasound and foetal MRI scanning allows the early detection of potential airway problems in babies and thus allows us a plan of management to avoid neonatal death. There is a 4.8 % incidence of a congenital abnormality seen on ultrasound scanning for pregnant mothers. Of these 4.8%, 2.5 % have a problem within the Head & Neck.

In the world medical literature, Complete Laryngeal Atresia, so-called CHAOS syndrome, (Congenital High Airway Obstruction Syndrome) there were 48 cases reported until 1993 and all these babies that were born died.

Between 1988 and 1994, 16 cases were reported and died, but since that time, since the evolution of the EXIT procedure there have been at least four or five survivors.

EXIT is Ex-Utero Intrapartum Treatment. It is a means of providing a safe oxygenation for the baby before delivery. The concept is that we deliver the heads

and shoulders only of the baby, through a cesarean section approach. And we are then able to perform some surgery, if necessary on the neck, or with intubation of a difficult airway. Then we deliver the baby, and then we divide the umbilical cord.

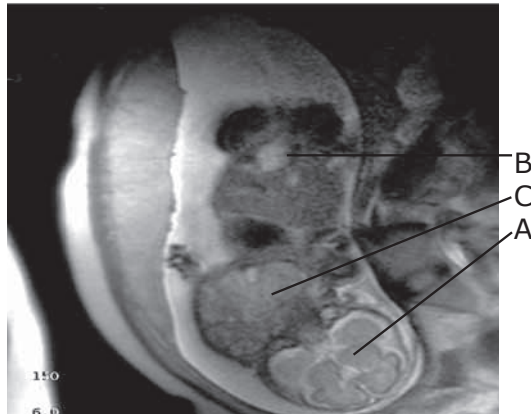
The indications for EXIT procedure are a mass compression of the foetal airway, seen on scanning, an abnormal airway anatomy, such as a very severe micrognathia or the CHAOS syndrome. We, at the Guy's & St Thomas' and Kings College Hospitals, until 2009, have been involved in about 20 cases: 10 EXITs for pre-natal diagnosed airway obstruction; one attempted intrauterine foetal tracheostomy and nine EXITs / balloon treatments for congenital diaphragmatic hernia (CDH). I am going to give you some examples. **Figure 1** shows a child with a large tongue tumor, which was in fact an embryonal rhabdomyosarcoma and we thought it was going to obstruct the airway posteriorly, so we proceeded with an EXIT at birth.

Figure 1. Diagnostic ultra sound (US) features. Large tongue tumor. Giant Foetal Head or Neck Mass. Obstructive lesion seen in relation to airway



Figure 2 shows a foetal MRI scan of a child who had - see the head here (A), the body here (B) and this is the tumor (C) This was a very large, congenital, thyroid teratoma, which was obstructing the airway and it was very abnormal larynx.

Figure 2.Foetal MRI. Congenital thyroid teratoma A=head/brain, B= body, C = Thyroid teratoma



The head & neck conditions which have been described in the medical literature as being diagnosable anti-natally and which may require an EXIT procedure are:

- cervical lymphangioma (cystic hygroma);
- lingual / pharyngeal lymphangioma;
- cervical teratoma;
- epignathus (teratoma arising from basisphenoid);
- laryngeal & tracheal atresia / stenosis (CHAOS);
- congenital thyroid goitre;
- tongue tumor;
- severe micrognathia.

In many of the patients, the most common diagnosis is a lymphangiomatous malformation (cystic hygroma, or lymphangioma). When it is only in the neck, it is rare that the airway is a problem. So, the EXIT procedure is not required. But when it is a hygroma involving the tongue and the pharynx and the larynx, this is when the anatomy is distorted and when we will plan an EXIT procedure.

What are the features on ultrasound? Obviously, one of the features that we see in an obstructive lesion; is the mass itself on the US scan, like the tongue that is in **Figure 1**. A giant foetal head or neck mass as an obstructive lesion will be seen in relation to airway. When there is complete obstruction of the airway, with laryngeal atresia, or CHAOS syndrome, then what happens is that the lungs expand (secondary dilated trachea & echogenic lungs), because the fluid which is formed into the lungs cannot be passed out to the amniotic fluid. The trachea then dilates and the lungs become hyperechogenic.

The problem which we have not yet solved is the situation with incomplete laryngeal /subglottis stenosis or laryngeal atresia with TOF (tracheo-esophageal fistula). These cases can present with no diagnostic features, because in this situation the fluid from the lungs comes out through the fistula and we don't see the dilation of the trachea. So, it is very hard for the ultrasound specialists to pick up the diagnosis and find it in utero.

Ultrasound (US) findings are very important in a complete laryngeal atresia. The atresia is present and the trachea is massively dilated and there is increased fluid in the lungs, increased echogenicity. And this pushes the diaphragm down and causes ascites. In our first case even cardiac compression occurred, which is life threatening.

What is the management, in general, when we have diagnosed a potential airway obstruction antenatally? We have to discuss it with the parents (parental counseling). In the UK the law allows termination of pregnancy routinely before 24 weeks and in rarer cases even at an older age if that is appropriate (termination option <24 weeks). But obviously the risks of proceeding with the birth or the long-term expectations if we proceed with the EXIT birth and the surgeries which might have to be performed in the future have to be discussed.

The multidisciplinary team who are involved in an EXIT birth delivery is very large: foetal medicine consultant, radiologist, obstetrician, obstetric

anaesthetist, pediatric ENT, pediatric surgeon, pediatric anaesthetist, neonatal intensivists, ODAs / theatre nurses / neonatal nurses.

When we are in the operating room (OR) there are very many people, all trying to become involved. This is how we perform the EXIT procedure: the concept is that the anaesthetists give a deep general anaesthetic to relax the maternal uterus and maintain the foeto-placental circulation. We deliver the head and the upper torso only through uterine incision; we can paralyze the baby's muscles with intra muscular paralysis; we use the foetal scalp to monitor the ECG & for pulse oxymetry; we do not ligate umbilical chord; we intubate or perforate trachea or perform a tracheostomy to establish an airway and then we deliver the baby. After this we can divide the chord.

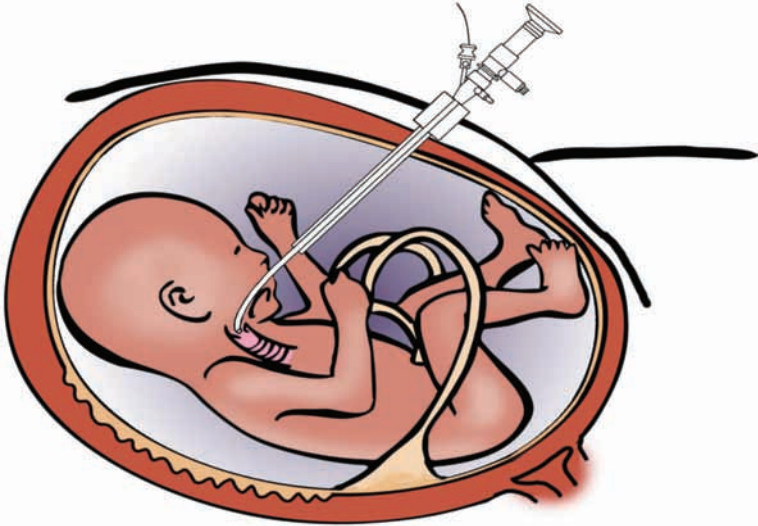
The maternal anaesthetic agents and their sequence which are typically used in our institution are as follows: isoflurane & N₂O; discontinue N₂O before hysterectomy; i.v. Vecuronium to maintain muscle relaxation; uterine stapling; after delivery – oxytocin The sequence to foetal anesthesia agents is: i.m. agents. establish airway, apply surfactant; then clamp & ligate chord. These methods should allow 20-60 minutes on placental support;

In one of our very early EXIT procedures (shown as a video in my presentation), and in fact it did not work very well, the obstetric surgeon did the hysterotomy and tried to get the baby's head out. He used a very small hysterotomy opening which is good - we try to avoid sucking out too much of the amniotic fluid. This is because if you reduce the pressure you can affect the placental circulation. That is what happened in this case, we lost too much amniotic fluid and lost placental circulation early. Normally we expect to have 60 minutes to 90 minutes to operate on the baby before delivery, with full oxygenation of the baby's brain. But it doesn't always work like that. So the head and the shoulder were delivered. And this is where sometimes "too many cooks spoil the broth", meaning that there were too many people in the disciplinary team. The neonatologist wants to be involved and show that he can do it, so he tried to intubate the baby, even though we, ENTs are the experts. And unfortunately he did not get the tube into the larynx because the anatomy was much distorted. We lost the placental circulation, the baby's heart rate was lower than forty and they tried to do something without success. But the reason we were here in this operating room (OR), assisting this case, as pediatric airway surgeons is that hopefully we imagined that we could restore the problem. I was then able to intubate the baby with an endoscope, very easily and then deliver the baby. Another thing we believe is important for successful EXIT is to keep the operating room temperature hot so that colder air does not provoke the foetal circulation changes too early.

Now I wish to comment briefly on a slightly newer development, the treatment of Congenital Diaphragmatic Hernias (CDH), which involves the same principles. I have to acknowledge my co-workers, particularly Prof. Kypros Nicolaidis from the King's College Hospital, a foetal medicine expert. The concept is that babies who have Congenital Diaphragmatic Hernias have poor development of their lungs and we want to establish the development by putting a balloon in the trachea and obstructing it (**Figure 3**). So, we are simulating the

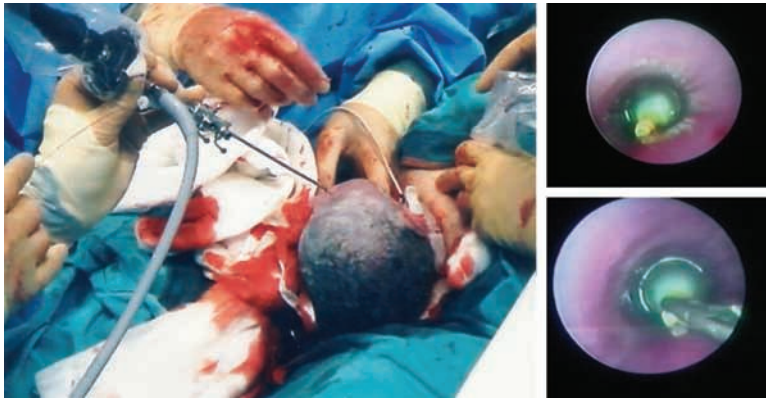
CHAOS situation, in which the trachea and the lungs would expand, and hopefully we can reach maturity.

Figure 3. Balloon tracheal occlusion for congenital diaphragmatic hernia (CDH)



CDH has an incidence of one in 3,000 live births. The problem is that the liver and the bowels will herniated into the thorax and the lungs do not develop. The prognosis overall is very poor for this condition. The management previously was either to terminate the pregnancy or an expectant treatment and to hope that the lungs are mature enough at birth for the baby to eventually survive. But the advent of foetoscopic surgery has allowed us the third choice. And the term FETO is what our research group has called this (foetal endoluminal tracheal occlusion procedure). We place a balloon in the trachea and then we have to retrieve it at birth. The concept is that the foetal lungs are net producers of fluid, and by blocking that fluid's escape, the lungs build up and compress the herniated contents down and the lungs become more mature. At birth we will have to retrieve the balloon.

Special instruments were developed, by Prof. Kypros Nicolaides to perform fetoscopy. **Figure 4** shows a 25-week-old foetus. We helped him with the laryngoscopy. This was the youngest bronchoscopy and laryngoscopy that I performed. We were able to see the vocal chord, inside the utero, and we began to see the tracheal rings, which means that we were in the trachea, no in the oesophagus. And then we did place a balloon, and the balloon was blown up and released. And it is left there for the lungs to mature. Then an EXIT birth is planned, when the mother is mature, and the balloon has to be removed.

Figure 4. 25-week-old fetus with congenital diaphragmatic hernia (CDH)

Only the most severe, life-threatening cases have been treated with this technique, and the control group to see if treatment works were people who, with the same severity of CDH on scanning parameters did not want to go ahead with the study. And they had a 90% mortality. We have a collaborative study that involve our group, in King's College Hospital, but also Prof. Jan de Prest in Belgium and Prof. Anne Debeer in Barcelona. So all these three institutions have been collaborating to perform the same surgery. The last 24 patients performed with this had a 50% long-term survival. Most recently we have placed the balloon earlier in the gestation and then burst it in utero by trans-uterine ultrasound controlled endoscopic techniques, so the team has avoided the need for the EXIT birth.

In conclusion, antenatal airway obstruction can be diagnosed with US and fetal MRI and allows a prediction of the problem and planning. Counseling allows us a choice of termination of pregnancy or an EXIT procedure, with therapeutic approaches to the airway to maintain a safe airway. In selected cases, this has led to an increase in survival. We have begun to demonstrate that congenital diaphragmatic hernias (CDH) can be treated by obstructing the airway to allow maturation and then relieving the obstruction at an EXIT procedure.

Recommended readings

1. "Prenatal diagnosis of airway compromise:EXIT (ex-utero intrapartum treatment) and foetal airway surgery" VMM Ward, K Langford & G Morrison Int. Journal of Paediatric OtorhinoLaryngology. 30 June 2000 (Vol. 53, Issue 2, Pages 137-141).
2. Bouchard S, Johnson MP, Flake AW, Howell LJ, Myers LB, Adzick NS, Crombleholme TM. The EXIT procedure: experience and outcome in 31 cases. J. Pediatr Surg. 2002 Mar;37(3):418-26.
3. Prenatal intervention for isolated congenital diaphragmatic hernia" Current Opinion in Obs & Gynae. Volume 2006,18(2):203-215.