1 **Anesthetic Management of an EXIT Procedure: A Novel Balanced**

2 **Approach**

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7 **Abstract:** *Ex Utero* Intrapartum Treatment (EXIT) procedures are therapeutic interventions for
8 fetuses with life-threatening airway abnormalities and/or other prenatally diagnosed congenital
9 malformations requiring immediate neonatal ECMO support. While certain anesthetic goals are
10 common among EXIT procedures, many different approaches to their management have been
11 described in the literature. Herein, we present a novel anesthetic approach to an EXIT procedure
12 for fetal micrognathia and retrognathia. We also review the indications and anesthetic
13 considerations for these procedures and highlight the need for multidisciplinary collaboration to
14 optimize clinical outcomes.

15 **Introduction**

16 The EXIT procedure may be best described as a staged or modified Caesarean section in which
17 the fetus is partially delivered from the uterus in order to secure the airway (or vascular access
18 for ECMO) while respiratory gas exchange is maintained via uteroplacental circulation.
19 Although the term “EXIT” had not yet been coined, fetal surgery on placental “bypass” was first
20 described in the late 1980’s for treatment of patients with pathologically large head and neck
21 malformations and high potential for airway embarrassment^{1, 2}. Since that time, EXIT

procedures have steadily gained interest and the indications for the procedure have grown. The anesthetic management of these procedures varies greatly, with both general and neuraxial techniques described in the literature. This case report details the first EXIT procedure performed at Brooke Army Medical Center—the largest military treatment facility (MTF) in the world—and our novel approach to anesthetic management.

Case Details

Our patient was a 23 year old, 84 kilogram primigravid active duty Army female referred to our institution at 30 weeks estimated gestational age for a higher level of prenatal care after a routine anatomy sonogram identified severe fetal micrognathia and retrognathia (Figures 1&2), as well as multiple limb anomalies and congenital heart defects. In consultation with pediatric otolaryngology, the obstetricians determined that an EXIT procedure was indicated, given the severity of the fetus' facial defects and the high likelihood of requiring invasive airway support due to her underlying cardiac condition. The patient was scheduled for an EXIT procedure at 38 weeks gestational age after pediatric cardiology concluded that the fetus' cardiac defects did not require more urgent delivery. The maternal preoperative anesthetic assessment was performed approximately two weeks prior to her scheduled procedure with both obstetric and pediatric anesthesiologists present to discuss maternal and fetal anesthetic considerations. This evaluation revealed a history of intermittent, symptomatic atrioventricular nodal reentrant tachycardia (AVNRT) for which she had undergone attempted radiofrequency ablation, with slight improvement in frequency of symptoms. She was otherwise healthy and had no personal or family history of anesthetic complications. Several additional collaborative and strategic

44 planning sessions were held amongst the care providers to discuss logistics and service-specific
45 roles and concerns with the multidisciplinary team to include obstetrics, maternal-fetal medicine,
46 obstetric anesthesiology, pediatric anesthesiology, pediatric otolaryngology and neonatology.
47 On the day of surgery, the patient was pre-medicated with sodium citrate 30 mL PO, ranitidine
48 50 mg IV and midazolam 2 mg IV. Upon arrival to the operating theatre and prior to induction of
49 general anesthesia, a continuous lumbar epidural catheter was placed for post-operative
50 analgesia. Following adequate pre-oxygenation and de-nitrogenation with the patient in the left
51 uterine displacement position, a rapid sequence induction was performed with fentanyl 100 mcg
52 IV, lidocaine 100 mg IV, propofol 150 mg IV and succinylcholine 100 mg IV. Following
53 uneventful intubation via direct laryngoscopy, an additional large-bore peripheral IV and a radial
54 arterial line were placed. General anesthesia was maintained with desflurane at approximately 1
55 MAC prior to uterine incision, with titration up to 1.5 MAC for the time from uterine incision
56 though full delivery of the fetus. Vecuronium was titrated as needed for muscle relaxation and
57 liberal use of intermittent fentanyl boluses was utilized to assist with fetal anesthesia during
58 airway manipulation. Upon skin incision, a bolus of nitroglycerin 40µg IV was administered and
59 a nitroglycerin infusion of $0.5 - 1 \mu\text{g kg}^{-1} \text{ min}^{-1}$ was initiated to enhance uterine relaxation. A
60 phenylephrine infusion was utilized to maintain maternal blood pressure within 20% of baseline
61 blood pressures.

62 After surgical exposure, the obstetricians confirmed adequate uterine relaxation and a
63 hysterotomy was performed. Following delivery of the fetus' head and right arm, the
64 neonatologist attempted to secure the airway via direct laryngoscopy with a Miller 0 blade,
65 followed by a videolaryngoscopy attempt with a GlideScope[®] AVL Preterm/Small Child blade
66 (Verathon Inc., Bothell, WA 98011). Both of these proved unsuccessful with no appreciable

view of the glottic opening. Pediatric otolaryngology then utilized direct rigid fiberoptic laryngoscopy and was able to successfully intubate the trachea. Fetal heart tones were monitored throughout airway manipulation via a sterile Doppler probe with no decelerations noted.

After securing the neonatal airway, the obstetricians resumed the Caesarean section. The total time from amniotomy to full delivery was 10 minutes. Following umbilical cord clamping, the nitroglycerine and phenylephrine infusions were halted and desflurane was reduced to 0.5 MAC with 50% N₂O. 40 units of oxytocin were added to a 500mL bag of crystalloid and slowly infused. Adequate uterine tone was reestablished with no further interventions required. Prior to emergence, her epidural was incrementally bolused with a total of 10 mL bupivacaine 0.25% to assist with postpartum analgesia.

After closure of the surgical incision, the patient was successfully extubated and underwent an uneventful post-anesthetic recovery on the post-partum ward. The total intraoperative maternal estimated blood loss was 1000 mL with a total of 2500mL of crystalloid and 1000mL of 6% hydroxyethyl starch administered. After ensuring adequate pain control, her epidural was removed on postoperative day one. The neonate underwent successful tracheostomy placement on day of life 2 in the controlled setting of the OR with the pediatric anesthesiology and otolaryngology teams. She was subsequently transferred to a local children's hospital for further treatment of her congenital heart defects.

Discussion

The EXIT procedure is an increasingly utilized technique for fetuses with potentially life-threatening airway abnormalities and/or requiring ECMO support. Although fetal surgery on placental support began in the 1980s, the *EXIT* procedure was not formally described in the

literature until the mid-1990s³. Since that time, the indications for the EXIT procedure have increased significantly (Table 1).

The anesthetic management of patients undergoing this procedure has evolved, as well, with a variety of strategies described in the literature. Despite the many anesthetic approaches, however, key concepts remain the same. Most important is the maintenance of profound uterine relaxation to prevent placental separation, which facilitates continued uteroplacental gas exchange⁵ while the airway (or vascular access for ECMO) is secured. In the early 1990s, this was usually accomplished with deep volatile-based general anesthesia with MACs in the range of 1.5 – 2.5. Since that time, multiple other anesthetic approaches have been reported, many of them employing tocolytic agents (nitroglycerin, terbutaline, or magnesium) in place of or in combination with volatile anesthetics to achieve the necessary uterine relaxation. Nitroglycerin is the most commonly used tocolytic, with documented infusion rates ranging from 0.3 to 20 $\mu\text{g kg}^{-1} \text{ min}^{-1}$ depending on the primary anesthetic technique utilized^{6, 7}. In general, lower doses of IV tocolytic agents should be required when utilizing volatile anesthetics due to the profound tocolytic effects of these agents. Significantly greater doses are required for primary neuraxial techniques. Regardless of the technique utilized, close communication with the surgeons is vital to determine the adequacy of uterine atony.

Given that placental transfer of volatile anesthetics occurs rapidly⁸ and can cause significant fetal cardiac depression, there is an argument to be made for using a lower concentration of these agents⁹. This is especially true for fetuses with congenital heart defects such as our patient. Although the cardiovascular depression is unlikely to have profound consequences for short (<30 minute) procedures, there are instances in which longer periods of placental support are required¹⁰. In these circumstances, fetal monitoring with either pulse oximetry or fetal

112 echocardiography may be utilized to determine the degree of fetal cardiac depression¹¹. Some
113 institutions have advocated the use of total intravenous anesthesia until uterine relaxation is
114 required, thus limiting fetal exposure to volatile agents⁹. Another method of limiting fetal
115 exposure to volatile agents is the addition of nitroglycerin (NTG), which makes deep volatile
116 anesthesia unnecessary given its profound tocolytic effect on the uterus⁷. Employing a neuraxial
117 technique as the primary anesthetic eliminates fetal exposure to volatile anesthetics all together.

118 Regardless of the method of anesthesia utilized, the agents that provide the amount of uterine
119 relaxation required for these procedures also result in greatly diminished maternal vascular tone.
120 If left untreated, this can result in untoward maternal hypotension and deleterious uteroplacental
121 insufficiency. Thus, maintenance of maternal blood pressure is paramount and can be achieved
122 with either intermittent boluses or infusions of vasopressors such as phenylephrine or ephedrine.

123 The anesthesia team must also be mindful that the fetus may require anesthesia, as well, to
124 facilitate care. If the mother is under general anesthesia, this goal is most easily accomplished
125 via uteroplacental transfer of volatile anesthetics and opioids.¹². In the event that neuraxial
126 anesthesia is utilized as the primary anesthetic, maternal intravenous supplementation with
127 opioids or direct fetal anesthesia via intramuscular injection may facilitate optimal surgical
128 conditions¹³ and limit the fetal stress response.

129 Our balanced approach to the anesthetic management of our patient addressed all the
130 aforementioned points and enabled us to avoid potentially detrimental effects of relying on one
131 anesthetic agent. The combination of moderate doses of inhaled general anesthetics with
132 intravenous nitroglycerin provided adequate uterine relaxation, while allowing us to limit fetal
133 exposure to unnecessarily high concentrations of anesthetic gases. The depth of inhaled

anesthesia was enough, however, to avoid the need for additional direct fetal anesthesia. The epidural provided outstanding postoperative analgesia and allowed the mother to concentrate on the care of her child.

Conclusion

The EXIT procedure is an increasingly used technique since its inception in the late 1980s. These cases provide unique challenges for the anesthesiologist and require a thorough understanding of the physiologic changes of pregnancy, uteroplacental physiology and the effects of selected pharmacologic agents. We believe that our balanced anesthetic approach of conventional volatile anesthetic depth (1 – 1.5 MAC) along with an infusion of an easily titrated tocolytic agent (i.e. nitroglycerin), judicious intraoperative monitoring and support of maternal hemodynamics reliably provides optimal surgical conditions while limiting potentially detrimental side effects. Our multidisciplinary approach also facilitates patient care and ideal operating conditions by coordinating perioperative care of both the parturient and the fetus/neonate.

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Table 1 *Indications for EXIT Procedure* (Adapted from ⁴)

Fetal Neck Masses – Teratoma, Hemangioma, Goiter

Lung Anomalies – Congenital Pulmonary Airway Malformation, Bronchopulmonary Sequestration

Mediastinal Masses – Teratoma, Lymphangioma

Micrognathia

Congenital High Airway Obstruction Syndrome – Tracheal or laryngeal atresia

Reversal of tracheal clipping

EXIT-to-ECMO

EXIT-to-separation for conjoined twins

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