Repair of Congenital Diaphragmatic Hernia during Extracorporeal Membrane Oxygenation

ROBERT D. TRUOG, M.D.,* JAMES A. SCHENA, R.R.T.,† MARC B. HERSHENSON, M.D.;‡ BABU V. KOKA, M.D.;§ CRAIG W. LILLEHEI, M.D.§

Extracorporeal membrane oxygenation (ECMO) is a form of prolonged cardiopulmonary bypass used to support newborns with life-threatening respiratory failure. This therapy is offered in at least 50 centers throughout the United States, with more than 2500 patients listed in the national Neonatal ECMO Registry.† Recently in our institution five newborns with congenital diaphragmatic hernia (CDH) required surgical repair during ECMO. These patients presented unique anesthetic challenges not previously described.

MATERIALS AND METHODS

Recent evidence suggests outcome may be improved when newborns with CDH are medically stabilized prior to surgical repair.1 These infants are considered stable if and when their oxygenation index (mean airway pressure [cm H₂O] × FiO₂/PaO₂ [mmHg]) is less than 0.4.2 Patients who cannot be stabilized with maximal conventional therapy are begun on ECMO support. ECMO is discontinued prior to surgical repair if and when relatively low levels of mechanical ventilation (peak pressure ≤ 30 cmH₂O, rate ≤ 30 breaths/min, FiO₂ ≤ 0.3) result in acceptable arterial blood gases (PaO₂ ≥ 60 mmHg, PaCO₂ ≤ 50 mmHg). Those who do not meet these criteria within 1 week have the diaphragmatic hernia repaired while receiving ECMO. From May 1988 through January 1989, five full-term newborns with CDH required surgical repair during ECMO.

The ECMO circuit has been described previously.2 Briefly, venous blood is drained by gravity from the right atrium to a small collapsible reservoir that buffers against slight fluctuations in venous return (fig. 1). Sustained decreases in venous return result in reservoir collapse, simultaneous triggering a microswitch and automatically shutting down the pump. Heparin and other fluids are administered into the reservoir. ECMO blood flow is provided by an occlusive roller pump. The oxygenator is a silicon membrane envelope separating fresh gas from blood. Gas exchange occurs by diffusion. The fresh gas flow is composed of three standard gases (air, 100% O₂, and 5% CO₂) that are blended together to provide the desired gas concentrations. Finally, the blood is warmed through a heat exchanger before being returned to the aortic arch via a cannula in the right common carotid artery.

Monitoring during CDH repair included an EKG, temperature probe, pulse oximeter, oscillometric blood pressure monitor, and a catheter in either an umbilical or peripheral artery. Ventilation was not required. A Mapleson circuit was used to provide CPAP and apneic oxygenation with 100% oxygen.

All patients received fentanyl before ECMO to provide sedation and to decrease their pulmonary vascular resistance.3 During ECMO the fentanyl infusion was continued and titrated to relieve discomfort and to minimize movement that could dislodge the vascular cannula. Elevations in blood pressure were managed with antihypertensive agents. Additional fentanyl and sufentanil were administered at the time of surgery to induce anesthesia and to blunt the cardiovascular response to surgical stimulation. Vecuronium was used for muscle relaxation. A heparin infusion of 80–110 U/h was used to maintain the activated clotting time between 150–200 s. Packed red blood cells were administered to keep the hematocrit above 40%, concentrated platelets were given to keep the platelet count above 100,000/ml, and fresh frozen plasma was used to keep the prothrombin time below 17 s. Additional colloids or crystalloids were administered when venous return into the ECMO circuit was inadequate to maintain ECMO pump flows between 250–400 ml/min. Mean blood pressure was maintained between 45–55 mmHg.

RESULTS

Individual data for birth weight, duration of surgery, opioid administration, blood loss, and fluid requirements are shown in table I. All patients were sedated with fentanyl before the initiation of ECMO at an average rate of 15 µg·kg⁻¹·h⁻¹ (range: 7–21 µg·kg⁻¹·h⁻¹). After 1

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* Instructor, Department of Anesthesia.
† Clinical Associate, Department of Anesthesia.
‡ Assistant Professor, Department of Anesthesia.
§ Instructor, Department of Surgery.

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Address reprint requests to Dr. Truog: Department of Anesthesia, MICU Office/Farley 2505, The Children's Hospital, 300 Longwood Avenue, Boston, Massachusetts 02115.

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‖ Robert Bartlett, M.D., written communication, April 1989.
week of ECMO therapy and immediately before surgery all patients remained sedated with a fentanyl infusion at an average rate of 24 μg·kg⁻¹·h⁻¹ (range: 13–37 μg·kg⁻¹·h⁻¹). Despite these large doses all of the patients were responsive to minimal stimulation with occasional spontaneous breaths. The mean intraoperative fentanyl dose was 199 μg/kg (range 69–321 μg/kg) with an additional mean sufentanil dose of 45 μg/kg (range 0–92 μg/kg). In addition, patients 2, 3, and 4 were given small doses of benzodiazepines and patient 4 also received 1% halothane via the endotracheal tube.

Despite receiving heparin, four patients had remarkably little blood loss (table 1). Patient 4 had minimal blood loss from repair of the hernia but had a substantial hemorrhage from a pulmonary laceration caused by chest tube placement. Intraoperative fluid requirements are listed in table 1.

None of the patients required vasopressors during the procedure. Four of the infants received hydralazine to reduce blood pressure, with patients 1 and 2 also requiring nitroprusside.

Significant anesthetic complications occurred in two patients. During transfer of patient 2 onto the operating room table, the venous cannula shifted resulting in a marked and sudden decrease in blood return to the reservoir. This was managed with rapid administration of volume and repositioning of the cannula under ultrasonographic guidance. During patient 4's operative repair, air was entrained into the venous side of the ECMO circuit during an episode of acute hypovolemia. The ECMO cannulae were clamped to prevent the air embolus from reaching the patient and conventional ventilation was initiated, resulting in arterial oxygen saturations of about 80%. The pump was manually operated to move the air to an access port where it could be aspirated. The patient was separated from ECMO for approximately 3 min with no apparent sequelae.

Only patient 4 eventually met criteria for the discontinuation of ECMO. This infant’s trachea was successfully extubated 25 days after separation from ECMO and he has since been discharged. ECMO was discontinued in the other patients when they were judged not to have a reasonable chance of survival. All of these patients died within several hours of being separated from ECMO.

**DISCUSSION**

We present our anesthetic experience with five newborns for repair of CDH during ECMO. The opioid doses we report are to our knowledge the largest in the anesthetic literature.

Fentanyl is the sedative of choice because of the large experience with this agents in newborns and because fentanyl has been shown to decrease pulmonary vascular resistance and increase survival in newborns with CDH as well as infants with pulmonary hypertension from other

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**TABLE 1. Repair of Congenital Diaphragmatic Hernia during ECMO**

<table>
<thead>
<tr>
<th>Patient</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth weight (kg)</td>
<td>3.5</td>
<td>3.0</td>
<td>2.4</td>
<td>3.8</td>
<td>2.5</td>
</tr>
<tr>
<td>Duration of surgery (h)</td>
<td>3.0</td>
<td>3.3</td>
<td>3.0</td>
<td>4.0</td>
<td>2.7</td>
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<tr>
<td>Opioids</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-ECMO fentanyl (μg·kg⁻¹·h⁻¹)</td>
<td>4</td>
<td>17</td>
<td>21</td>
<td>7</td>
<td>16</td>
</tr>
<tr>
<td>Preoperative fentanyl (μg·kg⁻¹·h⁻¹)</td>
<td>17</td>
<td>25</td>
<td>37</td>
<td>13</td>
<td>30</td>
</tr>
<tr>
<td>Intraoperative fentanyl (μg/kg)</td>
<td>69</td>
<td>31.7</td>
<td>321</td>
<td>79</td>
<td>210</td>
</tr>
<tr>
<td>Intraoperative sufentanil (μg/kg)</td>
<td>38</td>
<td>92</td>
<td>83</td>
<td>13</td>
<td>0</td>
</tr>
<tr>
<td>Estimated blood loss (ml)</td>
<td>10</td>
<td>40</td>
<td>30</td>
<td>750</td>
<td>30</td>
</tr>
<tr>
<td>Intraoperative fluids</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
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<td>Packed RBCs (ml/kg)</td>
<td>100</td>
<td>87</td>
<td>46</td>
<td>171</td>
<td>8</td>
</tr>
<tr>
<td>Colloid (ml/kg)</td>
<td>29</td>
<td>30</td>
<td>12</td>
<td>122</td>
<td>28</td>
</tr>
<tr>
<td>Crystalloid (ml/kg)</td>
<td>14</td>
<td>50</td>
<td>19</td>
<td>5</td>
<td>3</td>
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</tbody>
</table>
causes. Moderate amounts of midazolam are frequently given to limit the dose of opioid required. Although intrahalional anesthetics such as isoflurane could be given via the membrane oxygenator, the potential for nephrotoxicity from inorganic fluoride ion is a concern.

Despite the large doses of opioid administered, the infants are responsive to minimal stimulation and often spontaneously breathing. Possible explanations for the large opioid requirements include the increased volume of distribution contributed by the pump circuit, the binding of the opioids to the membrane oxygenator, and the development of tolerance to these agents. Since the volume of the circuit is about 400 ml, the volume of distribution of a 3-kg infant is increased by about 0.13 l/kg. Since the steady-state volume of distribution of fentanyl in newborns is 5.1 ± 1.0 l/kg, the volume of distribution of this agent is probably only modestly affected by the circuit volume. Both fentanyl and sufentanil are known to bind to the membrane oxygenator in substantial quantities and this uptake may increase dose requirements, especially during the first few days of ECMO. Infants treated with ECMO continue to be awake and often breathing after separation from the ECMO circuit (without a reduction in the dose of opioid), indicating that membrane binding is not the sole explanation for the large opioid requirement. Acute tolerance to fentanyl has been described in patients receiving continuous infusions and we consider this to be the most important reason for the large opioid requirements seen in these patients.

Although neuromuscular blocking agents could decrease sedative requirements, we prefer not to use them in the intensive care unit for the following reasons. First, severe intracranial hemorrhage occurs in 10% of ECMO patients with an overall incidence of 20–25% if minor hemorrhages are included. Frequent neurologic examination is the most timely monitor for this complication. Second, neuromuscular blocking agents can mask the development of seizures in the absence of continuous EEG monitoring. In addition, spontaneous respiration counteracts the development of atelectasis without the barotrauma associated with mechanical ventilation. Finally, even with EEG monitoring it is difficult to assess the adequacy of sedation in patients chronically relaxed with neuromuscular blocking agents.

The use of ECMO has several implications related to vascular access and monitoring. All drugs and fluids except platelets may be administered directly into the reservoir. Platelets adhere to the membrane oxygenator and are best given through a peripheral iv or central catheter. In an emergency platelets can also be given through a port distal to the membrane, but this carries the risk of arterial air embolism. Despite the use of heparin, peripheral iv catheters can usually be inserted without risk of hematoma formation. With regard to monitoring, pulse oximetry was frequently unreliable because of the combination of pulsatile and nonpulsatile flow. An oscillometric blood pressure device was a useful back-up to the intra-arterial catheter because of its accurate determination of mean arterial pressure despite weak pulsations.

The complications we observed were both related to decreased venous return to the pump circuit. This may cause cessation of extracorporeal circulation, and if pump shutdown does not occur, air entrainment and possible embolism. Decreased venous return may result from hypovolemia, malposition or kinking of the venous catheter, or surgical retraction that impedes venous flow. The management of this complication is fluid administration and/or correction of the obstruction.

Unlike patients undergoing cardiac surgery during cardiopulmonary bypass, infants receiving ECMO maintain a variable degree of intrinsic cardiac output. Interpretation of the patient's condition during ECMO requires an understanding of this unique physiology. For example, a decrease in arterial PaO₂ could reflect either an increase in cardiac output and pulmonary blood flow with increased shunting or a malfunction of the ECMO circuit. Inadequate anesthesia can result in arterial desaturation by the former mechanism. Proper management in this case includes additional anesthetic, β-blockade, an increase in pump flow, and/or increased ventilation of the lungs.

In summary, we described the anesthetic management of five infants for repair of CDH while on ECMO. Blood loss related to the hernia repair was minimal and no unmanageable complications were encountered.

REFERENCES

Hypoplastic Left Heart Syndrome: Anesthesia for Elective Noncardiac Surgery

Helen W. Karl, M.D.,*† Frederick A. Hensley, Jr., M.D.,* Stephen E. Cyran, M.D.,† Carl A. Frankel, M.D.,†‡ John L. Myers, M.D.‡§

Until this decade, hypoplastic left heart syndrome (HLHS, fig. 1A) was uniformly fatal. However, advances in surgical management of this lesion have improved the outlook for these infants. Currently, a two-stage procedure is the most common form of surgical intervention.1,2 In the neonatal period, the palliative first stage is performed to ensure unobstructed pulmonary venous return and systemic outflow, and includes a systemic to pulmonary artery shunt to regulate pulmonary blood flow (Norwood Stage 1, fig. 1B). It is followed by a Fontan operation at 1–3 yr of age when pulmonary vascular resistance is low.2 Survival after Stage 1 ranges between 60% and 70%,1 and the oldest survivors of both stages of repair are now 10 yr of age. Although most of these infants are free from other congenital anomalies,2,3 they can be expected to present for procedures commonly considered routine for pediatric patients.

Reviews of the anesthetic management of patients with HLHS4–6 focus on that for repair of the cardiac anomaly; there have been no reports of anesthesia for noncardiac procedures after first-stage palliation. Many of the perioperative concerns in these patients are not different from those in other patients with complex congenital heart disease and systemic to pulmonary artery shunts. Maintenance of stable shunt flow is central to the anesthetic management of all these patients.

CASE REPORT

An 8-month-old 6.5-kg female infant presented for elective bilateral medial rectus muscle recessions with left lateral rectus resection. She was 4 kg at birth, the product of an uncomplicated term pregnancy. In the neonatal period she was noted to have a heart murmur, echocardiographic findings of HLHS, and significant strabismus. On day 9 of life, she underwent Norwood Stage 1 palliation of her cardiac anomaly. Postoperative echocardiograms showed good ventricular function, but her course was complicated by pneumonia and bronchospasm. She was discharged home at 7 weeks. Her only medication was digoxin.

After discharge she developed mild tachypnea (50–60/min), diaphoresis with feeding, acrocyanosis with vigorous crying, and moderate hepatomegaly. She was hospitalized once for viral pneumonitis. Additional of diuretic and captopril to her cardiac medications decreased her congestive heart failure, and she grew steadily along a growth curve just below the 5th percentile for age. By the time of her preoperative evaluation for correction of severe esotropia (70 prism diopters), she was active, vigorous, and eating well. Medications included digoxin 30 μg po bid, diuril 60 mg po bid, and captopril 1 mg po bid. Her blood pressure was 120/70 mmHg, with a regular heart rate of 115–150 beats/min. She was not tachypneic and had minimal central and peripheral cyanosis at rest (peripheral oxygen saturation, SpO₂ 84–85%). On auscultation, her second heart sound was single, with a grade 2–3/6 continuous shunt murmur over the anterior precordium. Her lungs were clear. The liver edge was palpable just below the costal margin. Her hematocrit was 47% and serum electrolytes were within normal limits. The preoperative chest x-ray showed stable borderline cardiomegaly with near-normal pulmonary vasculature, and her ECG demonstrated right ventricular hypertrophy unchanged since discharge. An echocardiogram performed 3 months preoperatively and just prior to instituting diuril and captopril showed normal ventricular function, trivial tricuspid valve insufficiency, mild pulmonic insufficiency, a widely patent interatrial communication, and well-functioning systemic to pulmonary artery shunt.

On the morning of surgery, she received her usual cardiac medications and atropine 0.13 mg im on call to the operating room. She was monitored with an automatic blood pressure monitor (Dinamap®), a pulse oximeter (Nellcor®), ECG, precordial stethoscope, and esophageal temperature probe. Her vital signs were unchanged from the preoperative examination. A 22-G catheter was inserted in a peripheral vein and oxygen was administered by mask prior to induction. Gentamicin (12 mg) and ampicillin (325 mg) were given for endocarditis prophylaxis. An initial dose of 25 mg of thiopental (3.8 mg/kg) did not significantly change her systolic blood pressure or oxygen saturation. An additional 25 mg of thiopental in small divided doses was given during induction as required. She received 0.1 mg/kg of pancuronium and the trachea was intubated with a 5.5-mm ID uncuffed endotracheal tube. Anesthesia was maintained with air, oxygen, and halothane. FIO₂ was decreased to keep SpO₂ between 80% and 85%; the inspired halothane concentration was titrated to maintain systolic