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Veno-Venous Extracorporeal Membrane Oxygenation: Anesthetic Management for Massive Intracranial Hemorrhage in H1N1 Infection

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Abstract

Background: Extracorporeal membrane oxygenator (ECMO) use is dramatically increasing in recent years. This case report describes a patient on veno-venous (VV) ECMO for H1N1 who underwent emergent craniotomy twice for intracranial hemorrhage. Case presentation: A 38-year-old male presented to a community hospital for worsening shortness of breath. He had experienced cough, malaise and fatigue for two weeks prior to presentation. On arrival, his arterial oxygen saturation was 64%. He was placed on oxygen via non-rebreather mask and started on Tamiflu plus antibiotics. He was intubated for worsening respiratory failure. Despite maximal ventilator settings, the arterial oxygen saturation was approximately 90%. He was placed in the prone position and nitric oxide was initiated. Severe acute respiratory distress syndrome (ARDS) secondary to influenza was diagnosed by viral PCR, clinical presentation, and diagnostic imaging. Within 24 hours of his intubation, a decision was made to initiate veno-venous (V-V) ECMO for respiratory support. Five days following the initiation of ECMO, asymmetric pupils and a nonreactive right pupil were noted. A massive right frontal intraparenchymal hemorrhage with midline shift and downward uncal herniation was found on computed tomography (CT). A decision was made to surgically intervene. He was taken to the operating room for immediate right frontal craniotomy and clot evacuation under general anesthesia. Conclusion: With the dramatic increase in ECMO use, anesthesiologists are encountering patients on ECMO in the operating room with more frequency. When the situation does arise, it is imperative that the anesthesiologist is knowledgeable about ECMO and how to appropriately administer anesthesia for these critically ill patients. Challenges

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confronting the anesthesiologist with ECMO patients include managing bleeding or coagulopathy, ventilation and oxygenation, volume status, transporting and positioning these patients, and altered pharmacokinetics of anesthetic drugs.

Keywords

Venovenous ECMO, Extracorporeal Membrane Oxygenator, H1N1 Pneumonia

1. Introduction

During the 2009 H1N1 influenza pandemic in the US, 25% of patients admitted to the hospital with H1N1 required ICU care with 36% developing severe acute respiratory distress syndrome (ARDS) [1]. Veno-venous (VV) extracorporeal membrane oxygenation (ECMO) played a critical role and was employed in 34% of these patients in Australia and New Zealand [2].

There has been a dramatic increase in use of the ECMO for cardiac and respiratory failure in the last several years [3]. With this increase, anesthesiologists are encountering patients on ECMO in the operating room with more frequency. Historically, anesthesiologists have most often encountered these patients in the intensive care unit or in the cardiac operating room. Due to the success of ECMO, these patients are undergoing more aggressive management, including other noncardiac surgeries emergently. When these situations arise, it is imperative that the anesthesiologist is knowledgeable about ECMO and how to appropriately administer anesthesia for these critically ill patients. The following case was a patient who was placed on VV ECMO due to refractory ARDS secondary to H1N1 influenza and subsequently required emergency surgery for craniotomy twice during continued ECMO support.

2. Case Presentation

A 38-year-old male with no significant past medical history is presented to a community hospital for worsening shortness of breath. He had experienced cough, malaise and fatigue for two weeks prior to presentation. He showed no improvement with outpatient antibiotics and steroids and presented to the emergency department. On arrival, his arterial oxygen saturation was 64%. He was placed on oxygen via non-rebreather mask (15 L) and started on Tamiflu plus antibiotics. He then had a short trial of BiPAP but was ultimately intubated for worsening respiratory failure. Despite maximal ventilator settings, the arterial oxygen saturation was approximately 90%. He was placed in the prone position and nitric oxide was initiated. Severe ARDS secondary to influenza was diagnosed by viral PCR, clinical presentation and diagnostic imaging (**Figure 1**). Within 24 hours of his intubation, a decision was made to initiate veno-venous (V-V) ECMO for respiratory support. Prior to cannulation, he was given 5,000 IU of heparin as an IV bolus. The right femoral vein was cannulated with a 25 Fr Biomedicus (Medtronic) venous cannula which was advanced to the inferior vena cava for drainage of de-oxygenated blood. The right internal jugular was cannulated with a 21 Fr Biomedicus (Medtronic) arterial cannula which was advanced to the superior vena cava for the return of oxygenated blood from the ECMO circuit. The cannulas were connected to a Cardiohelp (Maquet) ECMO circuit and flow was initiated at approximately 5.5 LPM with appropriate blood gases exiting the circuit. Immediately after the initiation of VV ECMO, the ventilator settings were changed to volume control ventilation 6 cc/kg tidal volumes, 40% FiO_2, and PEEP of 10. The arterial oxygen saturation was 95% with VV ECMO support, despite significant decrease in ventilator support. A heparin infusion was initiated at 1000 units/hr and titrated to maintain an ACT of 160 - 220, as is our protocol. Serial therapeutic bronchoscopies were also performed.

Five days following the initiation of ECMO, asymmetric pupils and a nonreactive right pupil were noted. A massive right frontal intraparenchymal hemorrhage with midline shift and downward uncal herniation was found on CT (**Figure 2**). An immediate decision was made to surgically intervene, given his age and the potential reversibility of his condition with ECMO. The heparin drip was stopped and he was given fresh frozen plasma. He was taken to the operating room for immediate right frontal craniotomy and clot evacuation under general anesthesia. ECMO was continued without anticoagulation. Preoperative labs included, platelet count of 112,000, hemoglobin 6.8, PT 16, INR 1.35 and PTT 35. His creatinine was 3.0, he maintained an appropriate urine output and was not dialyzed.

The patient was transported to the OR from the ICU by a large multi-disciplinary team with great care taken to ensure hemodynamic stability and continuity of ECMO support. The team paid close attention to ensure the

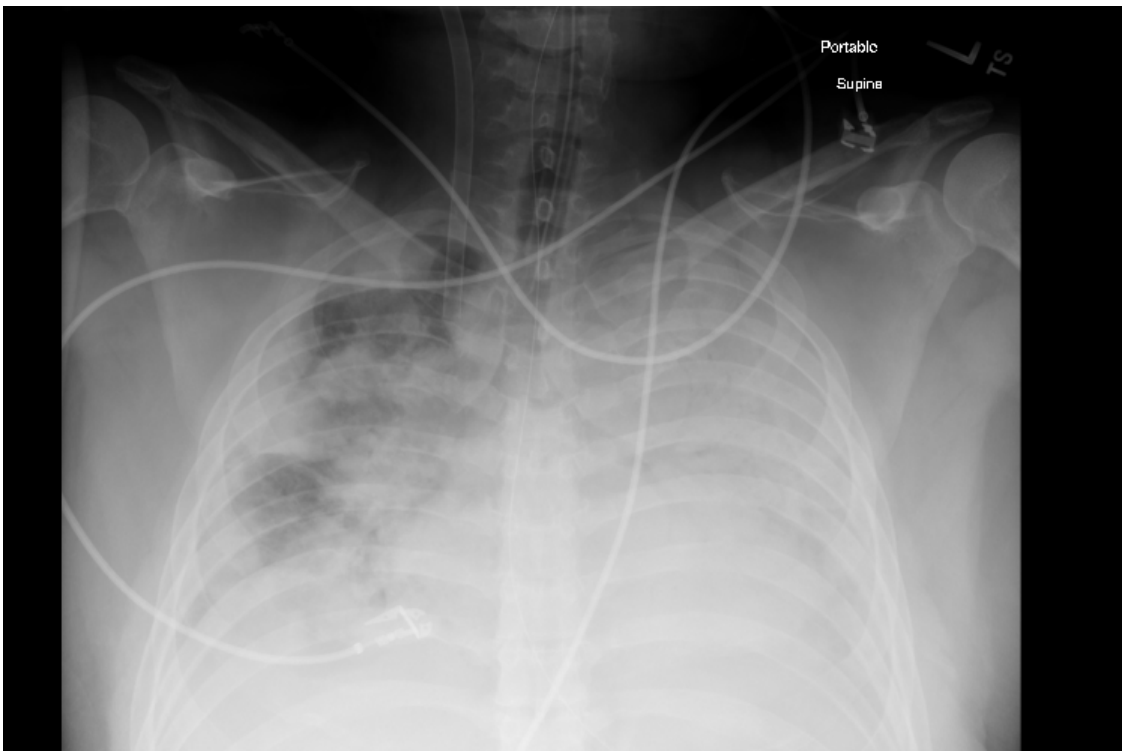

Figure 1. Chest X-ray of patient showing severe ARDS.

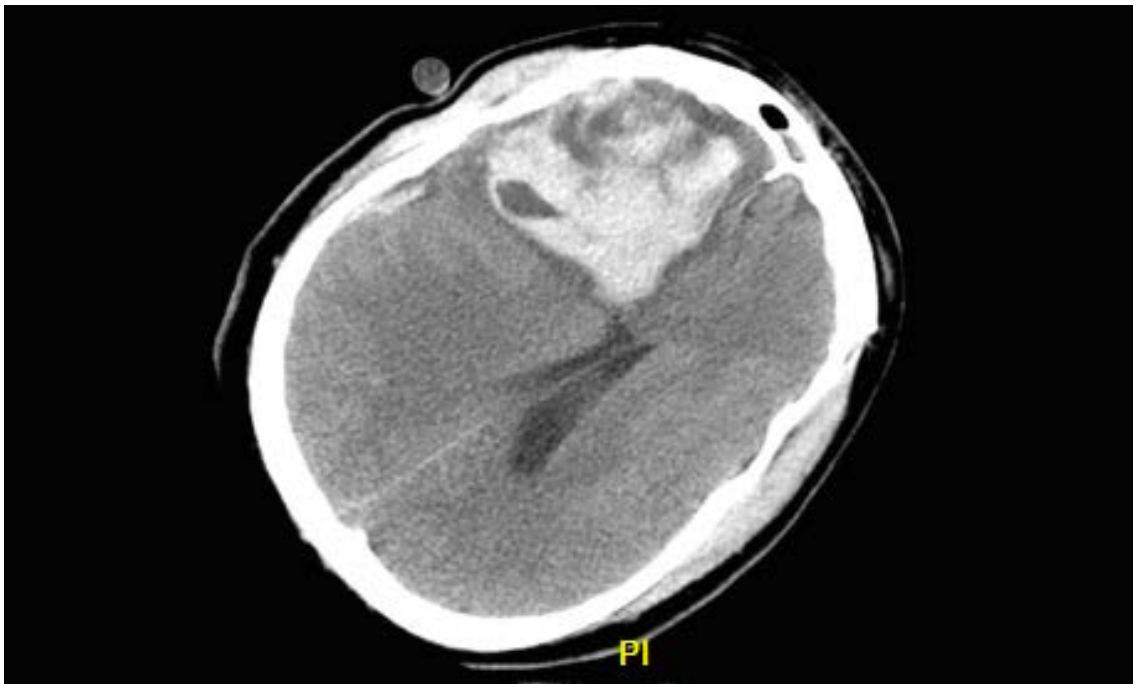

Figure 2. A massive right frontal intraparenchymal hemorrhage with midline shift and downward uncal herniation was found on CT.

ECMO cannulae were not for kinked or inadvertently dislodged. The patient was sedated in the ICU with a fentanyl infusion at 300 mcg/h and midazolam 14 mg/h. Once in the OR these drips were suspended and 2 mg of midazolam, 300 mcg of fentanyl, and 10 mg of vecuronium were given as a bolus. Sevoflurane was adminis-

tered. Positioning for the craniotomy was meticulous to obtain good surgical exposure without obstructing the ECMO IJ catheter. The patient was ventilated during the surgery at a PEEP of 12, RR 21 and tidal volumes of 200 - 400 cc. Protamine 20 mg was administered intraoperatively for an ACT of 141. Two units of fresh frozen plasma and 1 unit of packed red blood cells were transfused. He was carefully transported back to the intensive care unit by the same team. ECMO was continued without anticoagulation.

The patient continued to bleed and the following day the patient was taken back to the operating room for recurrent right intracerebral hemorrhage**.** During this surgery the anesthesia team chose to continue the fentanyl and midazolam infusions at the above rates and also gave 2 mg of lorazepam and 20 mg of cisatracurium. The clot was again evacuated and an intracranial pressure monitor was placed under general anesthesia. The prognosis was dismal and the patient was not expected to survive. Given this information, the family decided to withdraw care and discontinue ECMO after 237 hours of support.

3. Discussion

There has been a dramatic increase in use of the ECMO for cardiac and respiratory failure in the last several years. Between 1996 and 2007 there were approximately 100 cases per year voluntarily submitted to the Extracorporeal Life Support Organization (ELSO) registry. During 2009-2012, there was an increase to 480 - 846 cases per year. In 2009, there were 237 adult cases of respiratory failure with H1N1 influenza treated with ECMO, with 159 surviving (67%) reported to ELSO [3]. The overall ICU and hospital mortality of ARDS in patients receiving standard care without ECMO is higher than 40% [4].

This case illustrates several key points to keep in mind to safely and effectively deliver anesthesia to a patient on ECMO. Challenges confronting the anesthesiologist with ECMO patients include managing bleeding or coagulopathy, ventilation and oxygenation, volume status, transporting and positioning these patients, and altered pharmacokinetics of anesthetic drugs.

Bleeding is a common complication of ECMO and a hallmark of poor outcome, either due to withdraw of ECMO support due to uncontrolled bleeding or due to a hemorrhagic complication [5]. Often bleeding is disproportionate to the degree of coagulopathy or thrombocytopenia. ECMO circuits are often heparin coated but still require low-level heparin infusions parenterally not only to maintain circuity patency and functionality, but also to prevent systemic end organ damage from microthrombus, fibrin deposition, or an intracardiac clot [6]. The thromboembolic risks are lower with VV ECMO than with veno-arterial (VA) ECMO because any thrombus “thrown” from the circuit during VV ECMO enters the right atrium instead of the aorta (*i.e.*, brain, coronaries). Still, typically a heparin bolus is given intravenously at the time of ECMO cannulation and then an infusion is started once postoperative bleeding has been controlled, aiming for an aPTT of 50 - 80 s or ACT 160 - 220 [5]. An aim to keep platelets greater than 80 × 109/L is acceptable [6]. Lower degree of anticoagulation or even no anticoagulation for a period of time might be necessary if life-threatening hemorrhage exists [7]. ECMO support uniformly leads to thrombocytopenia, disseminated intravascular coagulopathy and renal dysfunction, which alter the function of the remaining platelets. This along with the use of anticoagulation leads to hemorrhagic complications [8]. There is continuous activation of the complement cascade due to contact with the ECMO circuit. Platelets then adhere to surface fibrinogen and aggregate. Correction by platelet transfusion produces only a temporary increase in platelet number [9] [10]. The anesthesiologist has the difficult task to balance the risk of thrombotic complications related to ECMO versus the bleeding risk. This is determined in a case by case basis, balancing the risks and benefits of transfusion.

Patients on VV ECMO should be monitored for systemic oxygenation and perfusion using the same parameters that would be used if they were not being supported with VV ECMO. Variables such as arterial and venous oxygen saturation, oxygen extraction, and lactate trending are all useful variables for monitoring these patients. The use of regional oximetry is often used as well. During VV ECMO, it is important that mechanical ventilation be decreased to low tidal volumes, low inspiratory pressures and exposed to lower oxygen concentrations to limit iatrogenic trauma and to allow the lungs to begin the healing process [11]. FiO_2 on the ventilator should be weaned to 40% and PEEP should be maintained at 5 - 10 cm H_2O and not altered in response to hypoxia. Low plateau pressures and tidal volumes should be used to minimize iatrogenic trauma. Often a SpO_2 of 85% and PaO_2 of 40 mm Hg are acceptable [12]. While *monitoring* of the VV ECMO patient’s oxygenation and perfusion may be similar to a non-ECMO patient, the *treatment* may be dramatically different. The temptation to increase the settings on the mechanical ventilator on a poorly oxygenated VV ECMO patient should be avoided whenev-

er possible. Instead, the ECMO settings and ECMO blood flow should be maximized prior to considering increases in the mechanical ventilator. If the patient's cardiac output is inadequate, leading to hypoperfusion, inotropes or other methods of increasing output must be considered, as VV ECMO does not directly provide cardiac support.

A thorough understanding of oxygen delivery is crucial to the treatment of patient oxygenation. A lower SpO_2 (*i.e.*, 75%) may be tolerated, provided that the hemoglobin is high enough to provide adequate oxygen deliver to the tissues. Conversely, a SpO_2 of 90% may *not* be adequate for an anemic patient. While many clinicians are comfortable tolerating anemia during VV ECMO, some authors recommend maintaining the hematocrit is kept around 40% while others cite a goal of >5% above normal [12] [13]. When deciding to transfuse the anesthesiologist must weigh the benefits of improved oxygen delivery with the risks of the transfusion [12]. While there is no universally accepted algorithm to determine the level of oxygen delivery that should be provided to these patients, it can be individualized to your specific patient based on parameters such as lactate, mixed venous oxygen saturation, and oxygen extraction. Carbon dioxide removal is usually not an issue because CO_2 removal via VV ECMO is more efficient than oxygen addition due to the higher solubility and faster diffusion properties of carbon dioxide relative to oxygen. If carbon dioxide is an issue, permissive hypercapnia is acceptable just as it would be for ARDS.

ECMO blood flow can be very volume dependent. The ECMO drainage cannula removes blood at significant negative pressures (typically −40 to −100 mm Hg), leaving the surrounding vascular tissue susceptible to getting sucked onto the tip of the cannula. This often leads to decreased flows, at least temporarily, until the tissue is allowed to release from the cannula. In addition to a drop in output, 'chatter' is seen in the venous tubing as the ECMO tubing swings back and forth while the cannulas suck down then release the surrounding tissue. Hypovolemia must be avoided due to avoid this venous 'chatter' and the resulting decreases in ECMO blood flow. Fluid or blood products are generally indicated to remedy this situation. With the additional fluids, patients may require diuresis to maintain a favorable fluid balance while closely monitoring ECMO blood flow [7]. Blood flow can also be affected by cannula malposition, pneumothorax, and pericardial tamponade. With any unexpected drop in ECMO blood flows, these causes should be investigated.

There is limited information on drug disposition during ECMO. Volume of distribution, protein binding, physico-chemical characteristics and physiologic changes all influence how particular medications will be influenced by the ECMO circuit [14]. There is significant sequestration of propofol, opioids and benzodiazepines in the circuit [13]. Greater than 50% reductions in concentrations of midazolam, lorazepam, and fentanyl have been shown during ECMO, while morphine does not seem to be affected [15]. The anesthesia team should not be surprised if an ECMO patient requires higher than usual doses of many anesthetic agents.

Transporting patients on ECMO can be a difficult and dangerous task. It requires a skilled team of providers that pay particular attention to lines and tubes. Dislodging a cannula or a break in circuit integrity could result in a fatal outcome. Positioning for surgery may also present challenges, particularly in situations such as our case with a jugular cannula and a craniotomy. Great care is required to provide an optimal surgical approach while maintaining the integrity and efficiency of the ECMO circuit. Other complications that anesthesiologists need to be aware of include air embolism and thromboembolism [7]. Mechanical complications related to ECMO include oxygenator failure, tubing rupture, pump malfunction, and cannula related problems. These require good communication with the ECMO specialist (*i.e.*, perfusionist, RT, or RN) when trouble-shooting. Fortunately, newer generation ECMO devices have greatly simplified ECMO and are much more convenient for transport [16].

4. Conclusion

H1N1 influenza can dramatically affect the health of previously healthy individuals. Extensive measures should be employed to save these patients' lives, including VV ECMO. ECMO use is dramatically increasing in recent years and the success rate is also improving. With the increasing use, anesthesiologists will encounter these patients with more frequency. Anesthesiologists must be adept at providing an anesthetic for these patients in the event that they require a surgical intervention.

Competing Interests

The authors declare that they have no competing interests.

Authors' Contributions

MK was the primary author of the manuscript. HR and RW oversaw the conceptualization, compilation and final edits. LL helped with the details of the case and final edits. CA primarily focused on the discussion section and gave insight from a perfusionist perspective. All authors read and approved the final manuscript.

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References

[1] Jain, S., Kamimoto, L., Bramley, A.M., Schmitz, A.M., Benoit, S.R., Louie, J., Sugerman, D.E., Druckenmiller, J.K., Ritger, K.A., Chugh, R. *et al*. (2009) Hospitalized Patients with 2009 H1N1 Influenza in the United States, April-June 2009. *The New England Journal of Medicine*, **361**, 1935-1944. http://dx.doi.org/10.1056/NEJMoa0906695

[2] Davies, A., Jones, D., Bailey, M., Beca, J., Bellomo, R., Blackwell, N., Forrest, P., Gattas, D., Granger, E., Herkes, R., *et al*. (2009) Extracorporeal Membrane Oxygenation for 2009 Influenza A(H1N1) Acute Respiratory Distress Syndrome. *JAMA*, **302**, 1888-1895. http://dx.doi.org/10.1001/jama.2009.1535

[3] Paden, M.L., Rycus, P.T. and Thiagarajan, R.R. (2014) Update and Outcomes in Extracorporeal Life Support. *Seminars in Perinatology*, **38**, 65-70. http://dx.doi.org/10.1053/j.semperi.2013.11.002

[4] Villar, J., Winston, B. and Slutsky, A.S. (1990) Non-Conventional Techniques of Ventilatory Support. *Critical Care Clinics*, **6**, 579-603.

[5] Marasco, S.F., Preovolos, A., Lim, K. and Salamonsen, R.F. (2007) Thoracotomy in Adults While on ECMO Is Associated with Uncontrollable Bleeding. *Perfusion*, **22**, 23-26. http://dx.doi.org/10.1177/0267659106074789

[6] Muehrcke, D.D., McCarthy, P.M., Stewart, R.W., Seshagiri, S., Ogella, D.A., Foster, R.C. and Cosgrove, D.M. (1995) Complications of Extracorporeal Life Support Systems Using Heparin-Bound Surfaces. The Risk of Intracardiac Clot Formation. *Journal of Thoracic and Cardiovascular Surgery*, **110**, 843-851. http://dx.doi.org/10.1016/S0022-5223(95)70119-2

[7] Marasco, S.F., Lukas, G., McDonald, M., McMillan, J. and Ihle, B. (2008) Review of ECMO (Extra Corporeal Membrane Oxygenation) Support in Critically Ill Adult Patients. *Heart, Lung and Circulation*, **17**, S41-S47. http://dx.doi.org/10.1016/j.hlc.2008.08.009

[8] Kasirajan, V., Smedira, N.G., McCarthy, J.F., Casselman, F., Boparai, N. and McCarthy, P.M. (1999) Risk Factors for Intracranial Hemorrhage in Adults on Extracorporeal Membrane Oxygenation. *European Journal Cardio-Thoracic Surgery*, **15**, 508-514. http://dx.doi.org/10.1016/S1010-7940(99)00061-5

[9] Stallion, A., Cofer, B.R., Rafferty, J.A., Ziegler, M.M. and Ryckman, F.C. (1994) The Significant Relationship between Platelet Count and Haemorrhagic Complications on ECMO. *Perfusion*, **9**, 265-269. http://dx.doi.org/10.1177/026765919400900404

[10] Robinson, T.M., Kickler, T.S., Walker, L.K., Ness, P. and Bell, W. (1993) Effect of Extracorporeal Membrane Oxygenation on Platelets in Newborns. *Critical Care Medicine*, **21**, 1029-1034. http://dx.doi.org/10.1097/00003246-199307000-00018

[11] Linden, V., Palmer, K., Reinhard, J., Westman, R., Ehren, H., Granholm, T. and Frenckner, B. (2000) High Survival in Adult Patients with Acute Respiratory Distress Syndrome Treated by Extracorporeal Membrane Oxygenation, Minimal Sedation, and Pressure Supported Ventilation. *Intensive Care Medicine*, **26**, 1630-1637. http://dx.doi.org/10.1007/s001340000697

[12] Tulman, D.B., Stawicki, S.P., Whitson, B.A., Gupta, S.C., Tripathi, R.S., Firstenberg, M.S., Hayes Jr., D., Xu, X. and Papadimos, T.J. (2014) Veno-Venous ECMO: A Synopsis of Nine Key Potential Challenges, Considerations, and Controversies. *BMC Anesthesiology*, **14**, 65. http://dx.doi.org/10.1186/1471-2253-14-65

[13] Chauhan, S. and Subin, S. (2012) Extracorporeal Membrane Oxygenation—An Anaesthesiologist's Perspective—Part II: Clinical and Technical Consideration. *Annals of Cardiac Anaesthesia*, **15**, 69-82. http://dx.doi.org/10.4103/0971-9784.91485

[14] Shekar, K., Roberts, J.A., Welch, S., Buscher, H., Rudham, S., Burrows, F., Ghassabian, S., Wallis, S.C., Levkovich, B., Pellegrino, V., *et al*. (2012) ASAP ECMO: Antibiotic, Sedative and Analgesic Pharmacokinetics during Extracorporeal Membrane Oxygenation: A Multi-Centre Study to Optimise Drug Therapy during ECMO. *BMC Anesthesiology*, **12**, 29. http://dx.doi.org/10.1186/1471-2253-12-29

[15] Harthan, A.A., Buckley, K.W., Heger, M.L., Fortuna, R.S. and Mays, K. (2014) Medication Adsorption into Contemporary Extracorporeal Membrane Oxygenator Circuits. *Journal of Pediatric Pharmacology and Therapeutics*, **19**, 288-295.

[16] Alwardt, C.M., Wilson, D.S., Alore, M.L., Lanza, L.A., Devaleria, P.A. and Pajaro, O.E. (2015) Performance and Safety of an Integrated Portable Extracorporeal Life Support System for Adults. *Journal of Extra-Corporeal Technology*, **47**, 38-43.