CRITICAL CARE MANAGEMENT OF SHEEP RECEIVING EXTRA-CORPOREAL MEMBRANE OXYGENATION DUE TO SMOKE INDUCED ACUTE LUNG INJURY (ECMO S-ALI) AND ACUTE SEPSIS

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Introduction

Extra-Corporeal Membrane Oxygenation (ECMO) is a form of life support where venous blood is drained from the patient to a gas exchange device (oxygenator), then becomes enriched with oxygen, has carbon dioxide removed and is returned to the patient’s circulation in the heart. Veno-venous ECMO (V-V ECMO) is utilised as a final resort in the critically ill patient with potentially reversible respiratory failure. It can significantly improve survival in this group of patients, but has associated problems. Studies have shown that cell damage and organ dysfunction occur during ECMO pathophysiology, along with increased blood transfusion, drug requirements and drug effects. The aim of this project is to understand and mitigate the complex problems associated with ECMO and smoke induced acute lung injury (S-ALI) during in-vivo instrumentation in a sheep model. Another arm of the study involves the monitoring and management of the anaesthetised animal with comparable induced severe infection, sepsis and inflammation. These studies have institutional animal ethics approval and are undertaken at the Medical Engineering Research Facility at The Prince Charles Hospital in Brisbane.

After instrumentation and induction of general anaesthesia, a standardized smoke injury is delivered to the animal. The cascade of events thereafter are monitored, recorded and managed. Serial blood samples are analysed, cardiovascular care and support are provided to maintain blood pressure with the use of ECMO, intravenous fluids, heparin anticoagulant and other drugs as required.

In the sepsis arm of the study, the animal is chronically instrumented. Lipopolysaccharide (LPS) is administered intravenously to cause widespread inflammation in the animal leading to septic shock. The animal is resuscitated using IV fluids, blood and other drugs as clinically indicated. Subsequent clinical parameters are managed as in the ECMO model.

ECMO saved many human lives during the swine flu outbreak. The knowledge from these studies is important in that it will help to improve the survival of patients on ECMO for future flu pandemics or similar acute lung diseases. This knowledge will also be useful in other forms of extra corporeal treatments such as cardiac bypass and haemodialysis. The knowledge from the acute sepsis part of the study will enable the understanding of optimum ways to resuscitate the patients with severe infection.

Anaesthesia, animal instrumentation and monitoring

A team comprising of a veterinarian and allied health professionals is involved and present during commencement of complex ECMO S-ALI and sepsis experiments, and remain on call for the duration of the experiment. ECMO S-ALI experiments run for nearly 30 hours. Our group has developed an ovine ECMO model.¹

Anaesthesia

Under a local anaesthetic, a central line and a pulmonary artery catheter are placed in the jugular vein. Baseline blood samples are routinely taken and the sheep are pre-medicated with midazolam and buprenorophine. Additional sheaths are placed in the opposite jugular vein to facilitate ECMO cannulation and intracardiac echocardiography. General anaesthesia is with induced with alfaxalone and the sheep is intubated and
ventilated. Anaesthesia is maintained by continuous infusions of alfaxalone/ketamine/midazolam. Buprenorphine is administered IV every six hours throughout the study period for ongoing analgesia. Mechanical ventilation is commenced using an intensive care ventilator with settings based on arterial blood gas (ABG) results.

Monitoring

Invasive arterial blood pressure (ABP) monitoring is ABG sampling achieved via the trans-facial artery. Physiologic variables are continually monitored with the aid multi-parameter platforms which in combination have capabilities to record continuous pulse oximetry (SpO₂), end tidal carbon dioxide (ETCO₂) electrocardiography (ECG), cardiac output (CCO), mixed venous oxygen saturation (SvO₂), central venous pressure (CVP), pulmonary artery pressure (PAP), core body temperature (BT) and derivatives for systemic vascular resistance (SVR) and stroke volume (SV) calculation. Measured variables are recorded every five seconds using proprietary software. Direct blood pressure measurement is not without problems; clotting in the catheter can occur, time is required to instrument the patient, the electronic equipment is expensive and potentially fatal complications can occur.²

ETCO₂ measurements that provide valuable information on the ventilatory status of the patient.²⁷ ETCO₂ measurement also provides earliest warning of serious hypotension, and very low cardiac output from the right side of the heart and detects apnoea and breathing circuit disconnections.²⁴ ABG analysis provides for arterial partial pressures of O₂ (P O₂) and carbon dioxide (P CO₂); and absolute values for oximetry including the concentrations of total blood haemoglobin (ctHb), oxygen saturation (SO₂), fractions of oxyhaemoglobin (FO₂Hb), carboxyhaemoglobin (FCOHb), methaemoglobin (FMetHb), deoxyhaemoglobin (FHHb) and foetal haemoglobin (FHbF). The ABG analysis provides information for blood acid-base status (pH), electrolytes (chloride, calcium, potassium and sodium ions) and metabolites (blood glucose and lactate). Ventilation data are recorded on a breath-by-breathe basis and readings for pulmonary static compliance are recorded from the ventilator at predetermined intervals.

Urine output is monitored via an indwelling urinary Foley catheter. Transudates and inflammatory fluids are collected in graduated receptacles connected to chest drains (and or peritoneal drains if indicated).

Monitoring of the macro and the microcirculation using side stream dark-field (SDF) imaging is often necessary in when investigating shock and mechanisms of organ injury. For examination of tissue effects of resuscitation with various fluids and blood products in ovine model of sepsis, tissue oxygenation is monitored by the insertion of oxygen probes directly into organs. Tissue perfusion is monitored by the insertion of Laser Doppler Flow probes body organs. Tissue metabolism is monitored by microdialysis.

Temperature, fluid, vasoactive drugs and electrolyte management

Continuous temperature recording is important in order to detect hypo- or hyperthermia in a timely manner and institute corrective measures.⁸ Animal patients lose body heat very rapidly when anaesthetised and precautions should be taken to avoid this.³⁷ Temperature is managed using a circulating warm water mattress attached to either the warm water pump cooler/heater. During ECMO, blood is heated in the oxygenator. Maintenance fluids are heated and delivered IV at 38–39°C at a rate of 2ml/kg/hr, or at 10ml/kg/hr during surgical interventions. Additional fluid boluses may be required to maintain blood pressure (BP) and cardiac output (CO) as it is clinically relevant to achieve mean arterial pressure (MAP) >65 mmHg and CO >3.0 L/min. Dopamine (5µg/kg/min) infusion is commenced if BP and CO with increased to normal systemic vascular resistance (SVR) occurs. Noradrenaline (0.01 mg/kg/hr) infusion is commenced if there is a decrease in BP, +/− a decrease in CO and a decreased in SVRI. These haemodynamic parameters are a rough guide only and may vary between experiments. Maintenance fluids are changed to 5% dextrose in normal saline if indicated. Potassium chloride solution (KCL) infusion at 5-20mmol/hr is supplemented as needed. In case of persistent dysrhythmias 20mmol of magnesium sulphate solution is given over 2-4 hours. Supplementation with calcium boluses (1000mg/sheep by slow IV) is required in times of hypocalcaemia and bicarbonate levels are corrected if the animal is critically ill and acidic depending on the bicarbonate deficit.

Sheep permit the collection of a unit of (approximately 400ml) into standard human blood collection bags to be used for resuscitation.¹⁰ Human cross-matching protocols have been modified for sheep, and our observations have detected 18.2% incompatibility between ovine packed red blood cells and potential recipient sheep. This highlights the importance of cross-matching especially in transfusion models.¹⁰
At completion of experiments, animals are euthanased with sodium pentobarbitone. Post-mortem examination is performed and organ samples are retrieved for further studies and the rest of the animal is disposed of routinely.

Acknowledgments


References

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