Observation of blood pressure guided fluid therapy in a bleeding-resuscitation animal experiment

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Abstract

The current protocol is a bleeding-resuscitation model intended to imitate the effects of severe blood loss and subsequent fluid resuscitation. The experimental subjects were Vietnamese pot-bellied pigs of both sexes weighing 33±4 kg. The animals underwent a 12-hours fasting pre-operatively but had free access to water. Anesthesia was induced by intramuscular injection of a mixture of ketamine (20 mg/kg) and xylazine (2 mg/kg) and maintained with a continuous iv. infusion of Propofol (50 µL/min/kg IV; 6 mg/kg/hr), while analgesia was maintained with intermittent nalbuphine (0.1 mg/kg). After endotracheal intubation, the animals were mechanically ventilated with a Hamilton C1 respirator (Hamilton Medical AG, USA). The tidal volume was set to 10 ml/kg, and the respiratory rate was adjusted to maintain the end-tidal carbon dioxide and partial pressure of arterial carbon dioxide within the range of 35–45 mmHg and the arterial pH between 7.35 and 7.45. The depth of anaesthesia was assessed by checking jaw tone. After induction of anaesthesia, catheters were inserted into the left jugular vein, left external carotid artery and the left femoral artery. For invasive hemodynamic monitoring, a transpulmonary thermodilution catheter (PiCCO, PULSION Medical Systems SE, Munich, Germany) was used. The femoral artery served as the site for arterial blood gas sampling, the central venous line was used for taking central venous blood gas samples and for the injection of cold saline boluses for the thermodilution measurements, whilst the carotid arterial catheter was used for draining blood. A transpubic catheter was placed into the urinary bladder for monitoring renal function. Animals were covered in scrubs and an external heating device was used to maintain physiological body temperature.

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Protocol

Step 1.

Anesthesia is induced by intramuscular injection of a mixture of ketamine (20 mg/kg) and xylazine (2 mg/kg) and maintained throughout the experiment with a continuous iv. infusion of Propofol (50 µL/min/kg IV; 6 mg/kg/hr). Analgesia is maintained with intermittent nalbuphine (0.1 mg/kg) administration.

Step 2.

After endotracheal intubation, the animal is mechanically ventilated with a Hamilton C1 respirator (Hamilton Medical AG, USA). The tidal volume is set to 10 ml/kg, and the respiratory rate is adjusted to maintain the end-tidal carbon dioxide and partial pressure of arterial carbon dioxide within the range of 35–45 mmHg and the arterial pH between 7.35 and 7.45.

Step 3.
Once the animal is under anesthesia and mechanically ventilated, catheters are inserted into the left jugular vein, left external carotid artery and the left femoral artery. The femoral artery serves as the site for arterial blood gas sampling, the central venous line is used for taking central venous blood gas samples and for the thermodilution measurements, whilst the carotid arterial catheter is used for draining blood.

Step 4.
A transpubic catheter is placed into the urinary bladder to monitor renal function.

Step 5.
As the instrumentation is complete, the animal has 30 minutes for equilibrium. After resting time, baseline measurements are taken.
These are the following:
- invasive hemodynamic measurements through transpulmonary thermodilution
- both arterial and central venous blood gas samples
- urinary output
- blood samples for laboratory tests

Step 6.
After the baseline measurements are complete, blood is drained from the arterial catheter placed in the left external carotid artery by direct suctioning with a 50 mL syringe, until the initial value of stroke volume index drops by 50%.

Step 7.
When the target SVI is reached (t_0), the animal has 20 minutes for equilibrium. After 20 minutes, all the measurements are repeated (i.e. hemodynamics, blood gases, blood samples, urinary output).

Step 8.
After reaching the target reduction of SVI, values of MAParetaken as targets of fluid replacement during the rest of the experiment. The difference between MAP_{tbsl} – MAP_{t0} is divided equally into four target values, which are aimed to be achieved in four steps during fluid resuscitation (t_{1-4}) to reach the baseline MAP by t_4. Fluid loading is carried out with boluses of balanced crystalloid Ringer Fundin (B. Braun AG., Melsungen, Germany). For practical reasons the total amount of crystalloid to be used for resuscitation is limited to 4.5 times the volume of the drained blood.

Step 9.
After reaching the first target value (t_1) during resuscitation, 10 minutes are allowed for equilibrium, then the complete measurement circle is repeated.

Step 10.
After reaching the second target value (t_2) during resuscitation, 10 minutes are allowed for equilibrium, then the complete measurement circle is repeated.

Step 11.
After reaching the third target value (t_3) during resuscitation, 10 minutes are allowed for equilibrium, then the complete measurement circle is repeated.

Step 12.
After reaching the fourth target value (t_4) during resuscitation, 10 minutes are allowed for equilibrium, then the complete measurement circle is repeated.

Step 13.
At the end of resuscitation, the animal is euthanized with Na-pentobarbital (120 mg/kg).