**Name of Journal: World Journal of Anesthesiology**

**ESPS Manuscript NO: 20753**

**Manuscript Type:** **MINIREVIEWS**

**Swine model in transplant research: Review of anaesthesia and perioperative management**

Morgaz J *et al.* Anaesthesia in swine model to transplants

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**Conflict-of-interest statement:** None.

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**Received:** June 22, 2015

**Peer-review started:** June 27, 2015

**First decision:** July 27, 2015

**Revised:** September 18, 2015

**Accepted:** October 16, 2015

**Article in press:**

**Published online:**

**Abstract**

Pigs are one of most common animal species to be used in biomedical models due to their many anatomical visceral similarities with humans, particularly with regards to transplantation. Despite this use, in many of the researches in which pigs are selected for transplantation, the anaesthesia used is an adaptation of human anaesthesia and presents some limitations such as a reduced analgesia a limited control in perioperative period. In this review we show some of the most important conditions in the preanaesthetic management and of swine as well as we review of anaesthetic protocols for the most common types of swine model of transplantation.

**Key words:** Swine; Anesthesia; Transplantation; Animal model; Perioperative management

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**Core tip:** Swine is a common model in research, especially in transplantation studies. A correct management and anaesthesia as well as knowledge of the different protocols in pigs are useful in performing these researches.

Morgaz J, Navarrete R, Granados MM, Gómez-Villamandos RJ. Swine model in transplant research: Review of anaesthesia and perioperative management. *World J Anesthesiol* 2015; In press

**INTRODUCTION**

Pigs are one of most common animal species used in biomedical models due to their many anatomical visceral similarities with humans, particularly with regards to metabolic or cardiovascular diseases and for liver, lung or heart transplantation[1-4]. These similarities have meant that pigs have become a potential species in xenotrasplantation in primates species[5-7]. Despite this resemblance, different anatomical and physiological aspects should be considered in order to perform a successful anaesthesia technique in swine, especially considering that in these researches major surgical procedures are usually performed. In addition, the perioperative care and management of pigs should be considered. In Table 1 are shown normal cardiorespiratory parameters of adult pigs during anaesthesia.

**PERIOPERATIVE CARE AND GENERAL CONSIDERATIONS**

As with other animals of research, an acclimatization period of 5-7 d prior to anaesthesia is necessary to reduce the depressant effect of transport or stress, which could alter the anaesthetic effects of different drugs or parameters related to the research. Before anaesthesia, a solid fast period of 24-48 h is recommended, but water must be maintained. The nervous and sometimes aggressive behaviour of pigs prevents venous cannulation before anaesthesia, and for this reason pre-anaesthetics must be administered by intramuscular route in almost all cases, alone or sometimes with anaesthetics such as ketamine. Athough piglets and some swine breeds have thinner skin, adult pigs usually have a wide tissue adipose and their skin is generally hard, and for this reason intramuscular administration is carried out using a large and thick needle (longer than 35-40 mm, over 18-20 G), to ensure that drugs are deposited in muscle. A longer onset and a softer effect of drugs are noted if anaesthetics are administered into adipose tissue. The most used anatomical locations for intramuscular administration are the lateral cervical muscle region (behind the ear), semitendinosus-semimembranosus muscle areas (posterior side of hindlimb), and the lumbar muscle area[8-10].

***Preanaesthetic protocol***

There are several anaesthetic protocols suitable for pigs, which include the combination of a hypnotic with a sedative and/or an analgesic. This approach provides a degree of anaesthetic suitable for the handling of pigs, although sometimes it is not enough for endotracheal intubation and an inhalation induction by mask is necessary to complete the anaesthetic induction. Oxygen administration *via* face mask is recommended because these combinations induce a variable degree of cardiorespiratory depression. Since the preanaesthetic combination is applied intramuscularly, dissociative agents such as ketamine and tiletamine (in commercial combination with zolazepam) are used[8,10-12]. Alphaxalone has also been evaluated as acting like a hypnotic in swine and when administered intramuscularly together with midazolam provides an excellent sedation, although it is only recommended for small pigs due to the large volume used[13].

Ketamine is the hypnotic habitually used because it can be administered intramuscularly and has a rapid onset, although due to its excitatory effects it must always be combined with a sedative and muscle relaxant[8,10,11]. Alfa-2 agonist sedatives (xylazine, medetomidine, dexmedetomidine) are widely used in both veterinary medicine and biomedicine, providing central sedative effects accompanied with muscle relaxation and analgesia[8,12,14]. Some frequent anaesthetic combinations in transplant researches with pigs are shown in Table 2.

Since the surgical techniques of transplant imply an aggressive approach or major procedures in most cases, at the time of designing an anaesthetic protocol it is important to consider the potential pain of the procedure during the surgery and the post-operative period. Transplantation surgery is major surgery that requires the use of an opioid analgesic in premedication and especially during the surgery, in which constant rate infusions of pure opiods (fentanyl or remifentanil), may be necessary[8,14]. Likewise, a multimodal approach must be used and f NSAIDs must be administered as carprofen[8-10].

***Anaesthetic induction and tracheal intubation***

Venous catheterization is often performed after the intramuscular premedication and often when tracheal intubation has been accomplished. The auricular veins are the most common access in pigs for the administration of additional intravenous anaesthetic drugs, fluid therapy and for obtaining venous blood samples. However, for transplantation surgery, central venous and arterial catheterizations are recommended (usually external jugular veins and femoral artery), because a major management of electrolyte and acid-base status is required. Moreover, a central venous access allows the monitoring of cardiac output control and pulmonary pressures. This advanced monitoring is especially indicated for research, when pigs must be maintained and controlled under intensive care conditions for several hours or days after surgery[8-10,15].

Usually it is not possible to perform the intubation after premedication since the metabolization of dissociatives is quick, so the induction of anaesthesia must be completed after the administration of the preanaesthetic combination in order to obtain an adequate relaxation of the laryngopharyngeal structures to perform a tracheal intubation. Propofol (2-5 mg/kg), can be administered intravenously if the ear vein has been catheterized (Table 3). Isofluorane or sevofluorane administration (3%-5%) in oxygen (2-4 L/min) *via* face mask is the most used technique. The use of neuromuscular blocks is initially inadvisable because tracheal intubation is difficult to perform and requires some experience[8-10,15].

Tracheal intubation can be performed in sternal, ventral or lateral recumbency, being a difficult procedure, especially in large pigs because the mouth cannot be opened sufficiently and laryngeal structures are not easily visible. In large pigs a specific straight laryngoscope (15-30 cm length) with a large blade is needed. The diameter of the endotracheal tube oscillates between 7 and 12 mm, depending of the size of the swine. In pigs above 25 kg, the use of a rigid or semi-rigid guide for tracheal tubes avoids bending and facilitates the intubation in sternal recumbency especially. To prevent laryngospasm during tracheal intubation, laryngeal irrigation with local anaesthetic (lidocaine or mepivacaine) is recommended[8-10,15].

***Anaesthetic equipment***

Pigs can be anaesthetized with human or veterinary anaesthetic machines. A corrugated and reservoir balloon must be selected according to the weight of the pig. Precision vaporizers of isofluorane, sevofluorane or desfluorane can be used attending to minimum alveolar concentration (Table 4), and several fraction of oxyegen can be set up. Mechanical ventilation settings for pigs are similar to other species and are shown in Table 5. For an adequate constant rate infusion of drugs (Table 6), a perfusor or infusion pump must be used.

**PIG AS A MODEL OF TRANSPLANT RESEARCH**

Swine is used extensively as a transplant model of different organs, but despite the complexity of these surgical procedures, in many researches of transplantation in pigs, special considerations are not taken into account and normal anaesthetic procedures are performed, but with important limitations.

***Renal transplantation***

In all the experimental kidney transplantation papers reviewed, even in very recently published papers, a lack in anaesthetic control and monitoring has been found. In most of the pig model studies, anaesthetic protocol is not even mentioned in a number of different papers[16-19]. Other studies describe the drugs and doses, but no description of the quality of anaesthesia or an evaluation of anaesthesia’s influence on patient evolution are mentioned. An intramuscular injectable mixture of a sedative and ketamine[20,21] or tiletamine-zolazepam[22] is the method most described for the induction of anaesthesia in pigs for kidney transplantation. The sedatives used were xylazine[20,22] or diazepam and azaperone[21]. Atropine was also added[20] to the injectable mixture to prevent bradycardia and reduce bronchial secretions. The authors another paper[23] used ketamine IM and thiopental IV directly as anaesthesia inductor agents without the previous use of sedatives. In this case the ketamine dose was increased to 5 mg/kg. Other papers administered propofol as a bolus for the induction of anaesthesia and to achieve an adequate depth of anaesthesia for tracheal intubation, either as a unique drug [22] or combined with fentanyl[21].

Atracurium and cisatracurium are frequently used in human kidney transplantation due to the fact that their duration of action is independent of either liver or kidney function, since other muscle relaxants, such as pancuronium, vecuronium or rocuronium, have a prolonged duration of action in patients with end-stage renal disease[24,25]. This is not a problem in experimental kidney transplantation if the recipient pig is healthy. Few authors describe the use of neuromuscular blockers in pigs. In[21] a bolus of cisatracurium after induction (15 mg/kg IV) was used and pancuronium (0.1 mg/kg IV) was used in[22], an experimental study. Anaesthesia maintenance in pigs is mainly performed using volatile agents, such as halothane 1%-2%[20], isoflurane[22,23] or sevoflurane 2%[21], although some other drugs have been used during anaesthesia maintenance to reduce the volatile agent requirements, such as remifentanil (0.08-0.1 mg/kg per hour)[21].Among all the reviewed papers, only[22] described that the depth of anaesthesia was assessed by a veterinary anaesthetist throughout the procedure and adjusted accordingly.

Pigs were under controlled ventilation during some experimental kidney transplantations[21-23].A description was found only when volume-controlled ventilation was applied, such as in[21] (minute volume 8 mL/kg; adapted according to blood gas analysis) or[22] (tidal volume 10-15 mL/kg; a peak inspiratory pressure of 25 cm of water; adjusted to achieve normocapnia, end-tidal carbon dioxide level 35-45 mmHg) studies. Fluids are needed in order to maintain optimum central venous pressure (CVP) and pulmonary arterial pressure. During a review of papers, no description of the type and rate of fluids used was found. Only[22] mentioned the use of Hartmann solution and Gelofusin and the internal jugular vein was used for this purpose.

With regard to perioperative pain control, drugs such as morphine, meperidine or oxycodone should be used with caution in patients with renal failure because these agents or their active metabolites depend on renal excretion and may accumulate[26,27].Fentanyl, sufentanil, alfentanil and remifentanil are safe for renal function[26,28-30]. Post-operative pain is controlled in different ways in humans, and it has been shown that the choice of intraoperative anaesthetic influences post-operative pain control, since patients receiving propofol had better recovery of psychomotor function and used patient-controlled analgesia more effectively than patients receiving halotane or isoflurane[31].No proper descriptions regarding perioperative and post-operative pain control have been found in the pig kidney transplantation review.

Hypotension may occur after unclamping the iliac vessels and reperfusion of the graft. Because the renal graft function depends on adequate perfusion, every effort should be made to avoid episodes of marked hypotension. Few studies describe the monitoring performed. Central venous pressure was measured using the internal jugular vein[22,23]. The brachial[23] or the auricular artery[22] were cannulated for blood pressure measurement. Oxygen saturation, ECG, temperature and end-tidal carbon dioxide were continuously measured during general anaesthesia[21-23]. In addition, full blood count, glucose, creatinine, urea, sodium, potassium, haemoglobin, alanine aminotransferase, aspartate aminotransferase and gamma-glutamyl transferase were measured in one study[21]. Some authors described that the recipient’s haemodynamic and metabolic alterations were treated, but no data were published. One paper[23] mentioned that they obtained effecctive anaesthetic maintenance until the experimental end point, and in the[22] study, that the vital signs of all pigs were stable during surgery and the post-operative observation period.

In animal models it has been shown that vessels in the transplanted organ seem to be more sensitive to sympathomimetics, and are thus more likely to compromise renal blood flow to the transplanted kidney, so strong alpha-adrenergic vasoconstrictors, such as phenylephrine, should be drugs used only as a last resort[32,33]. Drugs such as mannitol and dopamine have been used in human kidney transplantation but no references have been found to its use in pigs. Mannitol is usually administered to donors before recovery and to recipients just before unclamping the arterial blood flow, because it may give protection against ischaemic injury and induce osmotic diuresis. The use of a low-dose dopamine (2-3 mcg/kg per minute) to stimulate DA1 dopaminergic receptors in the kidney vasculature to induce vasodilation and increased urine output has been shown to be effective during kidney transplantation[34], whereas other studies have shown no significant improvement[35].

***Liver transplantation***

Although the initial liver transplantation studies included dogs, pig is the preferred species due to its physiologic and anatomic similarity with humans[36].

Azaperone is a butyrophenone that has been used as a sedative before general anaesthesia for liver transplantation, either as a sole agent at premedication[36,37] or in combination with other drugs, such as ketamine, diazepam or atropine[21,38,39]. Another pharmacological group used frequently for sedation at premedication in pigs undergoing liver transplantation is that of α2-adrenoceptor agonists, such as xylazine[40-44] or romifidine[45].Benzodiazepines are also used at premedication for muscle relaxation, generally combined with ketamine and/or a sedative drug since they are minor tranquillizers[21,38,41,46,47].There are authors that have used parasympatholytic drugs at premedication in pigs undergoing liver transplantation[39,41,43], the main use being as an excessive salivation inhibitor; it is unusual for bradycardia to be a problem in anaesthetized pigs[48].

The most common method is the use of a combination of drugs with different properties to induce a balanced premedication-sedation, such us the administration of sedatives with opioids[49].Furthermore, the administration of an analgesic before a painful stimulus optimizes the control of pain during the surgery procedure and reduces the dose of analgesic during the post-operative period. In general, mu agonists produce a more profound analgesia and they are recommended for moderate to severe pain and to reduce the necessity of anaesthetics[50]. Several authors have used an opioid at premedication in pigs prior to a liver transplantation[45,51].

Ketamine has been used at premedication in pigs undergoing a liver transplantation by several authors to immobilize the animal and to make easier its manipulation[21,39,40,42,45-47,51,52]. However, ketamine as a sole agent does not induce a surgical anaesthesia, so it would be necessary to combine it with opioids, benzodiazepines and/or sedatives[48].Another dissociative anaesthetic used in pigs is tiletamine, commercialized with zolacepam, a benzodiazepine[43,44].Like ketamine, it would be convenient to combine it with other sedative and/or analgesic agents to improve the quality or surgery anaesthesia [48].

For anaesthetic induction in pigs undergoing liver transplantation, several studies have used propofol[21,40,46,53,54], etomidate[39] or barbiturates[36,37,44,47].These drugs produce a faster onset of anaesthesia with short duration of action after the administration of a bolus. Other authors have used an inhalatory anaesthetic through a face mask for the induction of anaesthesia, after a satisfactory premedication[45,51].

Most of the authors have used inhalatory anaesthetics during the maintenance of anaesthesia in pigs undergoing a liver transplantation. Changes in the depth of anaesthesia are faster than with intravenous anaesthetics, with a faster recovery after the anaesthesia procedure[55].Isoflurane[36,39,40,42,51,54] and sevoflurane[21,41,44] are the anaesthetics most used. None of these anaesthetics are good analgesics, so many authors used them together with continuous infusion of fentanyl[21,36,40,44,45,56] or remifentanil[54].Other authors described the use of propofol in total intravenous anaesthesia (TIVA) during the maintenance of anaesthesia in pigs undergoing liver transplantation[52],even combined with a continuous infusion of fentanyl because propofol does not have analgesic properties[46,56,57].In addition, the pharmacological combinations for maintaining the anaesthetic in pigs during a liver transplantation has been described, with ketamine at 15 mg/kg per hour, fentanyl at 0.02 mg/kg per hour and midazolam at 0.9 mg/kg being used[38].

At induction and during the anaesthetic maintenance in pigs undergoing a liver transplantation it is common practice to the use of neuromuscular blocking agents such as pancuronium[36,39,41,45,51], atracurium[45,51], vecuronium[41] and cisatracurium[21].These agents are indicated to facilitate orotracheal intubation, and are administered together with hypnotic agents to avoid larynx spasm and to provide the fast control of the airway. Other indications included the prevention of spontaneous movement during the maintenance of anaesthesia, reducing the resistance to ventilation and easing surgical access during the surgical procedure[58].

During a liver transplantation, metabolic (acidosis) and cardiovascular changes (hypotension and bradycardia) are usual. To finish the experiences correctly, it is neccesary to understand these alterations, when they are produced and how to correct them. In human medicine, a liver transplantation procedure can be divided in three phases: (1) dissection phase, includes the lysis of adhesion and the removal of the damaged liver; (2) anhepatic phase, includes the implantation of donor liver; and (3) reperfusion phase, including the anastomoses, haemostasis and closure[59]. The ionized calcium levels can decrease during a liver transplantation, mostly during the dissection and anhepatic phases[60].The exogenous citrate from blood transfusion could be responsible for this low level of ionized calcium and calcium infusions may be required, such as calcium chloride and calcium gluconate[61].After reperfusion and with the beginning of the functionality of the transplanted liver, the haemostasis of calcium may be corrected and calcium supplementation may no longer be required.

During the anhepatic phase, the donor liver is implanted. If the surgery technique is infracaval interposition, there is a complete vascular occlusion by clamping the hepatic artery and porta, infrahepatic cava and suprahepatic cava veins. Because the inferior cava venous is blocked, a severe hypotension can develop. These haemodynamic effects depend on the patient, so it is advisable to place a previous temporary test clamp on the inferior vena cava to know the haemodynamic response of the animal before realizing the permanent vascular clamping during the anhepatic phase. Once the liver is positioned, the anastomosis of suprahepatic, infrahepatic and portal veins is completed in that order. The anastomosis of the hepatic artery is carried out before reperfusion or after the restoration of blood flow. During this phase hypocalcaemia and acidosis could be observed, so it is important to monitor these parameters closely. Avoid the aggressive infusion rate of fluids in this phase to maintain blood pressure, because this could result in overload of fluids resulting in cardiopulmonar compromise and liver and intestinal swelling. At the end of this phase the vascular clamps are removed and each anastomosis is observed for the detection of leaks[59].The withdrawal of the clamps from the portal vein allows blood flow from splanchnic circulation into the donor liver and is the beginning of the reperfusion phase. The most critical point in this phase is the immediate period after the vascular clamps are removed from the liver graft, mainly seconds or minutes after unclamping the portal vein, as is called as reperfusion syndrome[59]. A decrease in cardiac contractility[62],arrhythmias, bradycardia, severe hypotension and hyperkalemic arrest may be observed. The anaesthetic management must be directed at maintaining or recovering cardiovascular stability. The use of epinephrine, atropine, calcium or sodium bicarbonate could be neccesary[59]. Also, the use of methylene blue has been described as attenuating the haemodynamic changes during reperfusion syndrome[63].In this phase it is common for an alteration in the metabolism of glucose, and progressive hyperglycaeemia may ensue, due to the glycogenolysis by the donor liver, a decrease in glucose use and insulin resistence. In this phase it is possible that coagulopathy may develop, with resultant bleeding[59].

Severe coagulopathy and intraoperative loss of blood are significant problems in patients undergoing liver transplantation. This alteration in the homeostasis, mainly after receiving the donor liver, is multifactorial and inludes hyperfibrinolysis, depletion of coagulation factors, trombocytopenia and platelet dysfunction. The administration of fresh frozen plasma, red blood cells, platelets and cryoprecipitate are the main therapies for blood loss and coagulopatthy during liver transplantation. However, in humans, the use of these blood products during the liver transplantation has been significantly reduced in recent years due to an improvement in surgical technique, intraoperative management and in patient selection[59]. Currently, the administration of haemostatic agents, such as aminocaproic acid, tranexamic acid, etc., are being evaluated as adjunctive therapies[64-69]. It is important to restore diuresis during the procedure to facilitate fluid management and to protect the kidneys during the renal ischaemia in the anhepatic phase. Drugs used to maintain the urine output are loop diuretics, dopamine and mannitol[59].

Most of the pigs used in experimental procedures are euthanized at the end of the surgical procedure. However, some authors keep them alive to continue with the investigation. Authors of[41] described the use of buprenorphine during the post-operative period. Authors of[36] described this period in detail, evaluating the ingestion of the animals and the follow-up treatment with immunosuppression, antibiotics and buprenorphine as analgesic.

***Heart transplantation***

Porcine models have been used to study cardiovascular disease and transplantation, but have been associated with problems, such as friability of certain organs, anaesthesia difficulties, ventricular fibrillation and oedema[70].Cardiopulmonary bypass (CPB) models have been described only for two to four hours[71-73] or using swine models not of mature age or body weight, which cannot be considered as true adult size[74] and do not have the same responses to stress as do larger or mature swine [71].

Authors of one paper[75] described a swine model for long-term cardiopulmonary bypass using an adult pig weighing more than 80 kg. The anaesthesia protocol used for this model was very simple since ketamine and atropine sulphate were given intramuscularly followed by sodium pentobarbital intravenously to maintain a proper level of anaesthesia. Anaesthesia was maintained throughout the entire procedure using sodium pentobarbital in the mechanically ventilated pig. It maintained normothermic CPB and did not develop any previously described problems. Priming the CPB circuit with a combination of more adult blood than crystalloid solution possibly prevented the tissue oedema often seen in such procedures. HR, arterial pressures, urine production, hematocrit, electrolytes, glucose and lactate were within normal range throughout the cardiopulmonary bypass procedure and were not different from each other from the beginning to the end of CPB. Only the activated clotting time was maintained artificially higher than 1000 s. prior to the initiation of CPB and throughout the entire procedure and pO2 was also kept high. Modifications to the procedure, including a higher blood-to-crystalloid ratio in the priming solution, a slightly higher oxygen concentration in the circuit and maintaining the acid base status seemed to contribute to the success of this model.

Recently, the use of porcine cardiac xenografts has become more feasible because of the production of transgenic pig organs expressing human complement regulatory proteins on the endothelium, and continued surgical experimentation involving baboons will contribute to the understanding of the immunological basis for xenograft rejection. Orthotopic pig-to-baboon xenogeneic heart transplantation is the only accepted preclinical animal model for cardiac xenotransplantation[7].Anaesthetic management of the orthotopic pig-to-baboon model is complicated by ischaemia-reperfusion injury, the use of cardiopulmonary bypass and the additional immunological processes of xenogeneic transplantation.

A variety of animal experiments[76,77] and human studies[78-80] have investigated the benefits of different anaesthetic regimens in cardiac surgery, suggesting a protective effect of halogenated volatile anaesthetics on the myocardium by mimicking ischaemic preconditioning.

Santerre *et al*[81] described in detail a balanced anaesthetic technique for use in baboons undergoing abdominal porcine cardiac xenografting, and discussed intraoperative monitoring and treatment of the haemodynamic consequences related to infrarenal, aortic cross-clamping. The pharmacological techniques employed were found to be safe and reliable.

***Others types of transplant***

Swine has been used in other models of transplant such as pancreas[82],cornea[83],duodenum[84],uterus[85], vascularized composite allotransplantation[86], ureter-bladder[87] and lung[88],although in general the anaesthetic considerations are similar to most common transplant in pigs.

**CONCLUSION**

Swine is a common research model and a complete knowledge of the different protocols of anaesthesia and their perioperative care is important to develop transplant researches without complications. Pigs are excellent models of research and allow a more direct translation of results than laboratory animals, so they will continue to be frequently used in transplant research models.

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**P-Reviewer:** Mentes O, Wong KL **S-Editor:** Tian YL

**L-Editor: E-Editor:**

**Table 1 Normal cardiorespiratory parameters of adult and healthy pigs during anaesthesia**

|  |  |  |  |
| --- | --- | --- | --- |
| **Parameter** | **Range** | **Parameter** | **Range** |
| Heart rate (beats/min) | 50-100 | Temperature (ºC) | 36-38 |
| Respiratory rate (breaths/min) | 10-20 | Haemoglobin (g/dL) | 11-16 |
| Systolic arterial pressure (mmHg) | 80-140 | Et CO2 (mmHg) | 40-45 (mechanical ventilation) |
| Diastolic arterial pressure (mmHg) | 60-120 | Arterial pH | 7.38-7.50 |
| Mean arterial pressure (mmHg) | 40-70 | PaO2 (mmHg) | > 70-80 |
| Cardiac output (mL/kg per minute) | 60-140 | PaCO2 (mmHg) | 35-50 (mechanical ventilation) |

EtCO2: End-tidal of carbon dioxide; PaO2: Partial pressure of oxygen; PaCO2: Partial pressure of carbon dioxide.

**Table 2 Intramuscular preanaesthetic combinations for transplantation surgery in pigs**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Dissociative** | **Sedative** | **Analgesic (optional)** | **Time induction** | **Duration of anaesthesia**  |
| Ketamine(5-15 mg/kg), orTiletamine–zolazepam(5-10 mg/kg) | Medetomidine(5-20 mcg/kg), orRomifidine(60–100 mcg/kg), orDexmedetomidine(5-20 mcg/kg) | Morphine(0.3-0.5 mg/kg), orMethadone(0.3-0.5 mg/kg) | 5-20 min | 40-60 min |

**Table 3 Intravenous anaesthetic induction in pigs**

|  |  |
| --- | --- |
| **Anaesthetic** | **Intravenous doses** |
| Propofol | 2-5 mg/kg |
| Ketamine | 2-10 mg/kg |
| Tiopenthone | 5-15 mg/kg |

**Table 4 Minimal alveolar concentration of inhaled anaesthetics in pigs**

|  |  |
| --- | --- |
| **Anaesthetic** | **Minimal alveolar concentration** |
| Isoflurane | 1.2-2.0 |
| Sevoflurane | 2.2-3.5 |
| Desflurane | 8.3-10 |

**Table 5 Mechanical ventilation settings for pigs**

|  |  |
| --- | --- |
| Tidal volume | 10-15 mL/kg |
| Respiratory rate | 10-15 breaths/min |
| Maximum airway pressure recommendable | 20 cm H2O |
| Normocapnia (End-tidal CO2 concentration) | 40-45 mmHg |

**Table 6 Recommended doses of constant rate infusion of drugs in pigs**

|  |  |  |
| --- | --- | --- |
| **Drugs** | **Bolus intravenous** | **Constant rate infusion** |
| Fentanyl | 3-10 μ/kg | 10-30 μg/kg per hour |
| Remifentanyl | 10 μ/kg | 10-50 μg/kg per hour |
| Morphine | 0.1-0.3 mg/kg | 0.1-0.3 mg/kg per hour |
| Dexmedetomidine | 0.5-1 μ/kg | 0.5-1 μg/kg per hour |
| Medetomidine | 1-2 μ/kg | 1-2 μg/kg per hour |
| Ketamine | 0.5-2 mg/kg | 0.1-2 mg/kg per hour |
| Lidocaine | 2 mg/kg | 1-3 mg/kg per hour |
| Midazolam | 0.2-0.4 mg/kg | 0.2-0.4 mg/kg per hour |