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RESEARCH PAPER

Intravenous sufentanil-midazolam *versus* sevoflurane anaesthesia in medetomidine pre-medicated Himalayan rabbits undergoing ovariohysterectomy

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Abstract

Objective To compare physiological effects of sufentanil-midazolam with sevoflurane for surgical anaesthesia in medetomidine premedicated rabbits.

Study design Prospective, randomized controlled experimental study.

Animals Eighteen female Himalayan rabbits, weight 2.1 ± 0.1 kg.

Methods Premedication with 0.1 mg kg^{-1} medetomidine and 5 mg kg^{-1} carprofen subcutaneously, was followed by intravenous anaesthetic induction with sufentanil (2.3 μg mL^{-1}) and midazolam (0.45 mg mL^{-1}). After endotracheal intubation, anaesthesia was maintained with sufentanil-midazolam (n = 9) or sevoflurane (n = 9). Ovariohysterectomy was performed. Intermittent positive pressure ventilation was performed as required. Physiological variables were studied perioperatively. Group means of physiologic data were generated for different anaesthetic periods. Data were compared for changes from sedation, and between groups by ANOVA. Postoperatively, 0.05 mg kg^{-1} buprenorphine was administered once and 5 mg kg^{-1} carprofen once daily for 2–3 days. Rabbits were examined and weighed daily until one week after surgery.

Results Smooth induction of anaesthesia was achieved within 5 minutes. Sufentanil and midazolam doses were 0.5 μg kg^{-1} and 0.1 mg kg^{-1}, during induction and 3.9 μg kg^{-1} $hour^{-1}$ and 0.8 mg kg^{-1} $hour^{-1}$ during surgery, respectively. End-tidal sevoflurane concentration was 2.1% during surgery. Assisted ventilation was required in nine rabbits receiving sufentanil-midazolam and four receiving sevoflurane. There were no differences between groups in physiologic data other than arterial carbon dioxide. In rabbits receiving sevoflurane, mean arterial pressure decreased presurgical intervention, heart rate increased 25% during and after surgery and body weight decreased 4% post-operatively. Post-operative problems sometimes resulted from catheterization of the ear artery.

Conclusion Sevoflurane and sufentanil-midazolam provided surgical anaesthesia of similar quality. Arterial blood pressure was sustained during sufentanil-midazolam anaesthesia and rabbits receiving sevoflurane lost body weight following ovariohysterectomy. Mechanical ventilation was required with both anaesthetic regimens.

Clinical relevance Anaesthesia with sufentanil-midazolam in medetomidine premedicated healthy rabbits is useful in the clinical and the research setting, as an alternative to sevoflurane.

Keywords ovariohysterectomy, rabbit anaesthesia, sevoflurane, total intravenous anaesthesia sufentanil-midazolam.

Introduction

The rabbit (*Oryctolagus cuniculi*) is the third most common pet animal species undergoing anaesthesia in the United Kingdom (Brodbelt et al. 2008) and the third most commonly used laboratory animal species in Europe (European commission 2010). A surgical intervention routinely performed in female rabbits and which requires general anaesthesia is ovariohysterectomy. For largely unknown reasons, anaesthesia of rabbits carries a high mortality risk in comparison with dogs and cats (Brodbelt 2009). Possible anaesthetic risk factors in rabbits include; a high stress level, high prevalence of clinical and subclinical disease, small body size and relatively small lungs. Moreover, rabbits are not routinely endotracheally intubated and possibly are less carefully monitored during anaesthesia compared with cats and dogs (Brodbelt 2006). In addition, anaesthesia in rabbits has been studied less than in the aforementioned species.

Anaesthesia can be achieved with inhalation or injection of anaesthetic drugs. Some benefits of using inhalation anaesthesia are that most veterinarians are familiar with the technique and that anaesthetic depth can be precisely controlled. Sevoflurane (SEVO) has a lower blood: gas partition coefficient (0.7) than isoflurane (1.4), resulting in more rapid induction and recovery and possibly a greater ability to control anaesthetic depth. Total intravenous anaesthesia (TIVA) has the benefit of separating provision of anaesthesia from ventilation and reducing atmospheric pollution. If rapidly metabolized drugs which action can be antagonized are administered by target control infusion, adjustment of anaesthetic depth and time to recovery is rapid. High dose opioid anaesthesia provides cardiovascular stability in humans as well as in dogs (Bovill et al. 1984; Benson et al. 1987; Flecknell et al. 1989). In human cardiac surgery, sufentanil-based protocols have been shown to be superior to fentanyl in respect of cardiac output and haemodynamic stability during and after anaesthesia (Howie et al. 1991; Sato et al. 1995). In combination with midazolam, sufentanil has been shown to produce safe surgical anaesthesia in cardiovascularly compromised dogs suffering from gastric dilatation/volvulus (Hellebrekers & Sap 1991) and doses have been established in New Zealand White (NZW) rabbits premedicated with medetomidine (Hedenqvist et al. 2013; Larsson et al. 2014). Similarly to opioids, alpha-2-adrenergic agonists have been shown to reduce the surgical stress response in humans and dogs, which may prevent cardiac complications (Wijeysundera et al. 2009). Our aim was to compare sufentanil-midazolam (SUF-MID) anaesthesia with SEVO anaesthesia in medetomidine premedicated Himalayan rabbits regarding cardio-respiratory variables, lactate, glucose and recovery after surgery. Our hypothesis was that SUF-MID would have less effect on cardiovascular and metabolic variables than would SEVO.

Materials and methods

The study was granted permission from the regional ethics committee of animal experiments in Uppsala (C 83/12) and met the requirements of Swedish and EU legislation regarding the use of experimental animals.

Animals

Eighteen female Himalayan rabbits, with an age of 15 weeks and a mean ± SD body weight of 2.1 ± 0.1 kg were acquired from a certified breeder (Crl:CHBB[HM], Kissleg, Germany). According to standard health monitoring (Nicklas et al. 2002), the breeding colony was free from known rabbit pathogenic and opportunistic agents (rabbit haemorrhagic disease virus, rabbit rotavirus/rabbit corona virus, *Bordetella bronchiseptica, Clostridium piliforme, Pasteurella multocida*, *Salmonella* spp, endo- and ectoparasites, dermatophytes). The rabbits were housed in pairs in double cage systems (EC2, Scanbur Technology A/S, Denmark), with a total floor area of 0.86 m^2 and a combined hiding place/shelf. Autoclaved straw was used as bedding and the cages were cleaned once a week. Autoclaved hay and water *ad lib*, and a limited ration of pelleted feed (SDS Standard Rabbit, Special Diet Services, UK) was provided daily. The rabbits were acclimatised for two weeks, and during five days prior to surgery they were accustomed to handling by daily weighing. The light cycle was 08:00–17:00; the room temperature was 17 ± 1 °C and the humidity 50 ± 20%. The number of air changes was 15 $hour^{-1}$.