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RESEARCH PAPER

A comparison in dogs of medetomidine, with or without MK-467, and the combination acepromazine-butorphanol as premedication prior to anaesthesia induced by propofol and maintained with isoflurane

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Abstract

Objective To compare the haemodynamic effects of three premedicant regimens during propofol-induced isoflurane anaesthesia.

Study design Prospective, randomized cross-over study.

Animals Eight healthy purpose-bred beagles aged 4 years and weighing mean 13.6 ± SD 1.9 kg.

Methods The dogs were instrumented whilst under isoflurane anaesthesia prior to each experiment, then allowed to recover for 60 minutes. Each dog was treated with three different premedications given intravenously (IV): medetomidine 10 μg kg^{-1} (MED), medetomidine 10 μg kg^{-1} with MK-467 250 μg kg^{-1} (MMK), or acepromazine 0.01 mg kg^{-1} with butorphanol 0.3 mg kg^{-1} (AB). Anaesthesia was induced 20 minutes later with propofol and maintained with isoflurane in oxygen for 60 minutes. Heart rate (HR), cardiac output, arterial blood pressures (ABP), central venous pressure (CVP), respiratory rate, inspired oxygen fraction, rectal temperature (RT) and bispectral index (BIS) were measured and arterial and venous blood gases analyzed. Cardiac index (CI), systemic vascular resistance index (SVRI), oxygen delivery index (DO_2I), systemic oxygen consumption index (VO_2I) and oxygen extraction (EO_2) were calculated. Times to extubation, righting, sternal recumbency and walking were recorded. The differences between treatment groups were evaluated with repeated measures analysis of covariance.

Results HR, CI, DO_2I and BIS were significantly lower with MED than with MMK. ABP, CVP, SVRI, EO_2, RT and arterial lactate were significantly higher with MED than with MMK and AB. HR and ABP were significantly higher with MMK than with AB. However, CVP, CI, SVRI, DO_2I, VO_2I, EO_2, T, BIS and blood lactate did not differ significantly between MMK and AB. The times to extubation, righting, sternal recumbency and walking were significantly shorter with MMK than with MED and AB.

Conclusions and clinical relevance MK-467 attenuates certain cardiovascular effects of medetomidine in dogs anaesthetized with isoflurane. The cardiovascular effects of MMK are very similar to those of AB.

Keywords acepromazine, dog, general anaesthesia, haemodynamics, medetomidine, MK-467.

Introduction

A major aim during general anaesthesia is to maintain tissue perfusion and oxygenation. It is rarely possible to measure tissue perfusion directly, and instead, blood pressures are measured and inferences made about the tissue perfusion and the adequacy of oxygen delivery. However, the optimal tissue oxygen delivery depends on the cardiac output and arterial oxygen content.

Alpha-2-adrenoceptor agonists and neuroleptanalgesic combinations, such as acepromazine and butorphanol, are used widely for premedication in small animals. Medetomidine, a specific α_2-adrenoceptor agonist, is a potent sedative and analgesic agent with marked cardiovascular side effects (Vainio & Palmu 1989). It increases systemic vascular resistance due to vasoconstriction. This effect is accompanied by bradycardia and associated bradyarrhythmias, reduction in cardiac output and reduced oxygen delivery (Bloor et al. 1992; Pypendop & Verstegen 1998). MK-467 (also known as L-659,066) is a peripheral α_2-adrenoceptor antagonist that has been used experimentally to prevent or attenuate early cardiovascular side effects of α_2-agonists such as dexmedetomidine and medetomidine in dogs during sedation and thereby maintaining oxygen delivery (Pagel et al. 1998; Enouri et al. 2008; Honkavaara et al. 2008, 2011; Rolfe et al. 2012).

Acepromazine, in contrast to medetomidine, decreases arterial blood pressures and may lead to hypotension when used alone (Monteiro et al. 2007) or in combination with opioids (Stepien et al. 1995; Grint et al. 2010) during general anaesthesia. This is believed to be mediated via α_1-receptor antagonism (Ludders et al. 1983). However, irrespective of the hypotensive effects of acepromazine, the cardiac output and the oxygen delivery are well maintained during isoflurane anaesthesia in dogs (Monteiro et al. 2007).

The primary goal of the present study was to determine the impact of three premedication regimens on cardiovascular system function; including oxygen delivery during inhalant anaesthesia. The secondary aim was to compare the level of anaesthesia and the quality of recovery. We hypothesised that there would be significant differences in cardiovascular effects but not in the quality of sedation, anaesthesia and recovery between these three treatments.

Materials and methods

Animals

This study was approved by the National Animal Experiment Board of Finland. Eight healthy purpose-bred beagles (6 neutered males and 2 neutered females) aged 4 years and weighing 13.6 ± 1.9 kg were used in the study. Food was withheld for 12 hours before experiments, but water was provided *ad libitum*. Dogs were considered to be healthy based on a thorough clinical examination, a complete blood count and routine serum chemistry.

Instrumentation

Prior to each experiment, the dogs were instrumented under anaesthesia induced with propofol intravenously (IV) (maximum 6 mg kg^{-1}) and maintained with isoflurane. Dogs were allowed to recover from the anaesthesia for a minimum 60 minutes to ensure normal locomotor activity before baseline measurements were taken. During instrumentation, two cephalic vein 20 gauge cannulae (Terumo Europe N.V. Belgium), a 7 Fr double-lumen central venous catheter (CV-12702 Arrow International, PA, USA) and a dorsal pedal 22 gauge arterial cannula (Terumo Europe N.V., Belgium) were inserted aseptically and secured in place. The insertion site of the central venous catheter was premeasured so, that the final placing of the tip of the catheter would be at the level of the cranial border of the second rib at the costo-chondrial junction, and the correct place of the catheter was confirmed by the appearance of a typical central venous pressure waveform. The head of the dog was clipped, shaved and washed to ensure maximal contact of the bispectal index electrode. Acetated Ringer's solution was infused via the cephalic catheter at 10 mL kg^{-1} $hour^{-1}$ during instrumentation and the experimental period. The animals were kept on an electrical heating pad and covered with a blanket to maintain body temperature.

Study design

The dogs received three different IV premedicant regimens using a randomized cross-over design with a minimum washout period of 14 days between treatments:

- 10 μg kg^{-1} medetomidine (Dorbene 1 mg mL^{-1}, Laboratories Syva s.a., Spain) (MED).