Veterinary
Anaesthesia and Analgesia
Formerly the Journal of Veterinary Anaesthesia

Veterinary Anaesthesia and Analgesia, 2014 doi:10.1111/vaa.12220

RESEARCH PAPER

The cardiopulmonary effects of dexmedetomidine infusions in dogs during isoflurane anesthesia

Peter J Pascoe

Department of Surgical and Radiological Sciences, School of Veterinary Medicine, University of California, Davis, CA, USA

Correspondence: Peter J Pascoe, Department of Surgical and Radiological Sciences, School of Veterinary Medicine, University of California, Davis, CA 95616, USA. E-mail: pjpascoe@ucdavis.edu

Abstract

Objective To determine the cardiopulmonary changes associated with intravenous (IV) infusions of dexmedetomidine at equipotent isoflurane-dexmedetomidine concentrations compared with isoflurane alone.

Study design Prospective, randomized, crossover experiment.

Animals Six adult intact female mixed-breed dogs weighing (mean ± SD [range]) 23.3 ± 3.8 (17.8–29.4) kg.

Methods Anesthesia was induced and maintained with isoflurane in oxygen. Measurements of respiratory rate (f_R), heart rate (HR), systemic and pulmonary arterial pressures (SAP, DAP, MAP, MPAP), central venous pressure (CVP), pulmonary arterial occlusion pressure (PAOP), cardiac index (CI), left and right ventricular stroke work index (LVSWI, RVSWI), systemic and pulmonary vascular resistance index (SVRI, PVRI), arteriovenous shunt ($\dot{Q}s/\dot{Q}t$), oxygen delivery ($\dot{D}O_2$), oxygen extraction ratio (O_2ER), oxygen consumption, arterial and mixed venous blood gases, and arterial packed cell volume (PCV) were obtained 30 minutes after instrumentation at an end-tidal isoflurane concentration ($F_E'Iso$) of 1.73 ± 0.02% (1.3 MAC). Dexmedetomidine was administered IV at 0.5 or 3 μg kg^{-1} over 6 minutes followed by an infusion at 0.5 (LD) or 3 μg kg^{-1} $hour^{-1}$ (HD), respectively, with $F_E'Iso$ at 1.41 ± 0.02 (LD) or 0.72 ± 0.09% (HD). Measurements were taken at 10, 30, 60, 90, 120, 150 and 180 minutes after the start of the infusion.

Results The low dose produced significant decreases in HR, increases in SAP, DAP, CVP, MPAP, PAOP and LVSWI, but no change in CI. HD produced significant increases in SAP, MAP, DAP, CVP, PAOP, SVRI, LVSWI, O_2ER and PCV and significant decreases in CI and $\dot{D}O_2$. There were significant differences between treatments in HR, MAP, DAP, CVP, MPAP, PAOP, CI, SVRI, HCO_3^-, SBE, $\dot{D}O_2$, O_2ER and $\dot{Q}s/\dot{Q}t$.

Conclusions and clinical relevance Cardiopulmonary changes associated with LD were within clinically accepted normal ranges whereas HD produced clinically significant changes. The LD may be useful as an anesthetic adjunct in healthy dogs.

Keywords dexmedetomidine, dogs, intravenous infusion, isoflurane.

Introduction

The halogenated inhalant anesthetics cause significant depression of cardiopulmonary function and so there has been an interest in finding anesthetic adjuncts that would allow the use of decreased concentrations of these drugs. In dogs, fentanyl, nitrous oxide, ketamine and lidocaine have all been shown to reduce the dose of inhalant needed to maintain the same plane of anesthesia with a

resulting improvement in cardiovascular function (Steffey et al. 1975; Ilkiw et al. 1994; Boscan et al. 2005; Ortega & Cruz 2011). These drugs have antinociceptive properties and may benefit the animal during surgical procedures by contributing to an overall blunting of nociceptive input (Macintyre et al. 2010). The alpha$_2$-adrenergic agonists are also analgesics but have profound effects on the cardiovascular system at doses used commonly in veterinary practice (Pypendop & Verstegen 1998). Even at a dose of medetomidine at 1 μg kg^{-1} intravenously (IV) the cardiac index decreased to <50% of the baseline value (Pypendop & Verstegen 1998), when a dose in the range of 5–10 μg kg^{-1} is frequently used for premedication prior to general anesthesia. However, in human anesthesia the alpha$_2$-adrenergic agonists are commonly used at low doses with minimal effect on cardiac output and reduced likelihood of mortality, tachycardia or myocardial ischemia has been reported (Talke et al. 1995; Wijeysundera et al. 2009; Kabukcu et al. 2011).

The purpose of this study was to establish a dose of dexmedetomidine that would reduce the concentration of inhalation agent necessary to maintain anesthesia without severely decreasing cardiac output. When used as an IV infusion during anesthesia in dogs, medetomidine infusions have ranged from 0.2–12 μg kg^{-1} hour^{-1} (Kaartinen et al. 2010) and the cardiovascular effects reported have been dose related. Factors that may alter the cardiovascular response include prior administration of drug, loading dose and the rate at which it is administered, infusion rate and inhalant concentration. In Congdon et al. (2013), the dogs were premedicated with 10 μg kg^{-1} dexmedetomidine and the intraoperative infusions of dexmedetomidine had no further effect on the cardiovascular response. In Kaartinen et al. (2010), a low dose of medetomidine (0.2 μg kg^{-1} loading dose with a 0.2 μg kg^{-1} hour^{-1} infusion) had minimal effect on cardiovascular function, medetomidine (0.5 μg kg^{-1} hour^{-1}) induced small, but statistically significant effects, and higher dose rates resulted in increasingly depressant effects. In the latter study, the isoflurane concentration was maintained at the same level throughout the infusion, which may have altered the hemodynamic response.

The effect of dexmedetomidine on the minimum alveolar concentration (MAC) of isoflurane has been measured with infusion rates of 0.5, 1 and 3 μg kg^{-1} hour^{-1} that were documented to decrease MAC by 5–31%, 18%, and 42–59%, respectively (Pascoe et al. 2006; Kulka et al. 2012; Ebner et al. 2013). The aim of this study was to determine the cardiopulmonary effects of IV infusions of dexmedetomidine (a loading dose of 0.5 or 3 μg kg^{-1} followed by infusions of 0.5 or 3 μg kg^{-1} hour^{-1}, respectively) when administered with isoflurane at equipotent doses to 1.3 MAC. The hypothesis was that these two dose rates of dexmedetomidine administered at equipotent isoflurane concentrations would have no effect on cardiopulmonary function in dogs.

Materials and methods

This research was approved by the Institutional Animal Care and Use Committee. Six conditioned adult intact female dogs weighing 23.3 ± 3.8 kg were acclimated to the housing facility for 3 weeks. The dogs were assessed as being healthy based on physical, hematological and biochemical examinations. The dogs were fasted for 12 hours and water was available until the dogs were brought to the laboratory for the study. The study was carried out by one investigator and was a randomized, crossover design such that dogs were assigned to one treatment using a web based random assignment (www.randomizer.org) and then received the other treatment after a 2 week washout period.

A standard circle anesthetic system was used. The dogs were anesthetized with isoflurane using a mask to deliver 5% isoflurane in oxygen (5 L minute^{-1}). Once anesthetized the dogs were endotracheally intubated and allowed to breathe spontaneously and the oxygen flow rate was decreased to 1 L minute^{-1}. The dogs were placed in lateral recumbency. The endotracheal tube was equipped with a catheter whose tip was close to the distal end of the tube. This was used to draw end-tidal gas samples into a 6 mL glass syringe, by hand, for the measurement of end-tidal isoflurane concentration (F$_E$'Iso) using an infrared analyzer calibrated to 1/100th% (LB- 2 Medical Gas Analyzer; Beckman Instruments, CA, USA) as described previously (Steffey & Eger 1974; Steffey et al. 1994). In between these samples the catheter was connected to an analyzer (Raman gas spectroscopy, Rascal II; Ohmeda, UT, USA), which displayed the changes in carbon dioxide concentration with breathing as well as the concentrations of oxygen, nitrogen and isoflurane. This was used to monitor minute-to-minute changes but the only value recorded was respiratory rate (f_R, breaths minute^{-1}).

