RESEARCH PAPER

Effect of dexmedetomidine on the minimum infusion rate of propofol preventing movement in dogs

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Abstract

Objective To determine the effect of dexmedetomidine on induction dose and minimum infusion rate of propofol preventing movement (MIR_{NM}).

Study design Randomized crossover, unmasked, experimental design.

Animals Three male and three female healthy Beagle dogs weighing 10.2 ± 2.8 kg.

Methods Dogs were studied on three occasions at weekly intervals. Premedications were 0.9% saline (treatment P) or dexmedetomidine (1 μg kg^{-1}, treatment PLD; 2 μg kg^{-1}, treatment PHD) intravenously. Anesthesia was induced with propofol (2 mg kg^{-1} and then 1 mg kg^{-1} every 15 seconds) until intubation. Anesthesia was maintained for 90 minutes in P with propofol (0.5 mg kg^{-1} $minute^{-1}$) and saline, in PLD with propofol (0.35 mg kg^{-1} $minute^{-1}$) and dexmedetomidine (1 μg kg^{-1} $hour^{-1}$), and in PHD with propofol (0.3 mg kg^{-1} $minute^{-1}$) and dexmedetomidine (2 μg kg^{-1} $hour^{-1}$). The stimulus (50 V, 50 Hz, 10 ms) was applied to the antebrachium, and propofol infusion was increased or decreased by 0.025 mg kg^{-1} $minute^{-1}$ based on a positive or negative response, respectively. Data were analyzed using a mixed-model ANOVA and presented as mean ± standard error.

Results Propofol induction doses were 8.68 ± 0.57 (P), 6.13 ± 0.67 (PLD) and 4.78 ± 0.39 (PHD) mg kg^{-1} and differed among treatments ($p < 0.05$). Propofol MIR_{NM} values were 0.68 ± 0.13, 0.49 ± 0.16 and 0.26 ± 0.05 mg kg^{-1} $minute^{-1}$ for P, PLD and PHD, respectively. Propofol MIR_{NM} decreased 59% in PHD ($p < 0.05$). Plasma propofol concentrations were 14.04 ± 2.30 (P), 11.30 ± 4.30 (PLD) and 7.96 ± 0.72 (PHD) μg mL^{-1} and dexmedetomidine concentrations were 0.68 ± 0.12 (PLD) and 0.89 ± 0.08 (PHD) ng mL^{-1} at MIR_{NM} determination.

Conclusions and clinical relevance Dexmedetomidine (1 and 2 μg kg^{-1}) decreased propofol induction dose. Dexmedetomidine (2 μg kg^{-1} $hour^{-1}$) resulted in a significant decrease in propofol MIR_{NM}.

Keywords anesthesia, dexmedetomidine, dogs, minimum infusion rate, propofol.

Introduction

Total intravenous anesthesia (TIVA), as a balanced technique for maintaining a surgical plane of anesthesia, continues to be investigated in veterinary patients (Herbert et al. 2013). When compared with inhalation anesthesia, TIVA may enhance patient hemodynamics, reduce the incidence of postoperative nausea and vomiting, improve recovery quality and eliminate exposure to volatile anesthetics (Keegan & Greene 1993; Adams et al. 1994; Lauder 2015). An ideal drug for TIVA provides unconsciousness, muscle relaxation and antinociception; has a fast onset and rapid clearance; lacks cumulative effects; and is devoid of adverse properties (Schnider 2015).

Propofol has a favorable pharmacokinetic profile for TIVA in dogs, with a fast onset of action and rapid clearance (Nolan & Reid 1993). Nevertheless, the administration of propofol is associated with adverse effects such as dose-dependent hypotension, respiratory depression and apnea (Keegan & Greene 1993; Nagashima et al. 2000). In addition, because propofol lacks antinociceptive properties (Frölich et al. 2005), an analgesic agent should be added. Many TIVA protocols utilize multiple drugs to achieve unconsciousness, antinociception and muscle relaxation, and to decrease individual drug dose rates and, potentially, adverse drug effects (Mannarino et al. 2012).

The α_2-adrenergic receptor agonists are commonly used for premedication before anesthesia and to reduce the doses of induction and maintenance drugs (Vickery et al. 1988; Hellebrekers & Sap 1997). Dexmedetomidine, an α_2-agonist, has clinically important sedative, muscle relaxing and analgesic properties (Uilenreef et al. 2008; Gutierrez-Blanco et al. 2013). When used as a continuous rate infusion (CRI), dexmedetomidine caused a dose-dependent decrease in the minimum alveolar concentration (MAC) of isoflurane (Pascoe et al. 2006; Ebner et al. 2013; Acevedo-Arcique et al. 2014) and sevoflurane (Moran-Muñoz et al. 2014) in dogs. A CRI of 3 μg kg^{-1} $hour^{-1}$ was associated with a 24.8% decrease in the isoflurane end-tidal concentration necessary to perform ovariohysterectomies in dogs (Gutierrez-Blanco et al. 2013).

The minimum infusion rate (MIR) is analogous to the MAC of volatile anesthetics in that it is defined as the ED_{50} of an intravenous (IV) anesthetic agent that prevents purposeful movement in response to a noxious stimulus in 50% of subjects (Chambers & Hall 1987). The MIR required to prevent all movements, purposeful or nonpurposeful, is defined as the minimum infusion rate no movement (MIR_{NM}) and is considered to be more clinically applicable than the MIR (Reed et al. 2015; Davis et al. 2017).

The purpose of this study was to determine the effect of two doses of dexmedetomidine on the induction dose of propofol and, when subsequently administered as a CRI, the effects on the MIR_{NM} of propofol in dogs. It was hypothesized that dexmedetomidine would result in a dose-dependent decrease in the induction dose and MIR_{NM} of propofol.

Materials and methods

Animals

A total of six healthy, intact Beagle dogs (age, 3−5 years), three males and three females (weight, 10.2 ± 2.8 kg; mean ± standard deviation), were used in this study. Health status determination was based on the presence of normal findings on physical examination, and values for packed cell volume, total solids, blood glucose and lactate concentrations in the normal range. Food, but not water, was withheld for 12 hours prior to each anesthetic episode. The study protocol was approved by the Institutional Animal Care and Use Committee of the University of Tennessee (No. 2440).

Experimental design

Each dog was administered three treatments assigned using an unmasked, randomized crossover design (SAS, Version 9.4 TS1M3; SAS Institute Inc., NC, USA) with a minimum of 7 days between experiments.

The treatments were propofol alone (treatment P), propofol and low-dose dexmedetomidine (treatment PLD), and propofol and high-dose dexmedetomidine (treatment PHD). Treatment P consisted of premedication with 0.9% saline (Abbott Laboratories, IL, USA), induction of anesthesia with propofol (Propoflo; Abbott Laboratories), and maintenance with CRIs of propofol (starting at 0.5 mg kg^{-1} $minute^{-1}$) and saline (1 mL kg^{-1} $hour^{-1}$). Treatment PLD consisted of premedication with dexmedetomidine (1 μg kg^{-1}; Dexdomitor 0.1, Zoetis Inc., MI, USA), induction with propofol and maintenance with propofol (starting at 0.35 mg kg^{-1} $minute^{-1}$) and dexmedetomidine (1 μg kg^{-1} $hour^{-1}$). Treatment PHD consisted of premedication with dexmedetomidine (2 μg kg^{-1}), induction with propofol and maintenance with propofol (starting at 0.3 mg kg^{-1} $minute^{-1}$) and dexmedetomidine (2 μg kg^{-1} $hour^{-1}$). Dexmedetomidine doses for PLD and PHD CRIs were combined with saline and delivered at 1 mL kg^{-1} $hour^{-1}$. Treatments were administered IV.

Premedication and anesthesia

Blood was obtained by jugular venipuncture to provide baseline plasma concentrations for drug analysis and baseline laboratory values for packed cell