Veterinary Anaesthesia and Analgesia, 2006, **33**, 97–103 doi:10.1111/j.1467-2995.2005.00236.x

RESEARCH PAPER

Changes in the minimum alveolar concentration of isoflurane and some cardiopulmonary measurements during three continuous infusion rates of dexmedetomidine in dogs

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Abstract

Objective To measure the change in the minimum alveolar concentration of isoflurane associated with three constant rate infusions of dexmedetomidine.

Study Design Prospective, randomized, and blinded experimental trial.

Animals Six healthy 6-year-old Beagles weighing between 13.0 and 17.7 kg.

Methods The dogs received each of four treatments; saline or dexmedetomidine at 0.1, 0.5 or 3 μg kg^{-1} loading dose given intravenously (IV) over 6 minutes followed by infusions at 0.1, 0.5 or 3 μg kg^{-1} $hour^{-1}$, respectively. There were 2 weeks between treatments. The dogs were mask-induced with and maintained on isoflurane in oxygen. Acetated Ringer's (5 mL kg^{-1} $hour^{-1}$) and saline or dexmedetomidine (each at 0.5 mL kg^{-1} $hour^{-1}$) were given IV. Pulse rate, blood pressure, samples for the measurement of blood gases, pH, lactate, packed cell volume (PCV), total protein (TP) and dexmedetomidine concentrations were obtained from an arterial catheter. Sixty minutes after induction minimum alveolar concentration (MAC) was determined by intermittently applying supramaximal electrical stimuli to the thoracic and pelvic limbs. Cardiopulmonary measurements and arterial blood samples were collected before each set of stimuli. Statistical analyses were conducted with analysis of variance or mixed models according to the experimental design.

Results There was a significant decrease in the MAC of isoflurane associated with 0.5 and 3 μg kg^{-1} $hour^{-1}$ but not with 0.1 mg kg^{-1} $hour^{-1}$. Serum concentrations of dexmedetomidine were not measurable at the 0.1 mg kg^{-1} $hour^{-1}$ and averaged 0.198 ± 0.081 and 1.903 ± 0.621 ng mL^{-1} for the 0.5 and 3 μg kg^{-1} $hour^{-1}$ infusion rates, respectively. Heart rate decreased with increasing doses of dexmedetomidine while blood pressure increased. Packed cell volume increased at 3 μg kg^{-1} $hour^{-1}$ but not with other doses.

Conclusions and Clinical relevance Dexmedetomidine infusions decrease the intra-operative requirement for isoflurane and may be useful in managing dogs undergoing surgery, where the provision of analgesia and limitation of the stress response is desirable.

Keywords dexmedetomidine, heart rate, isoflurane, minimum alveolar concentration.

Introduction

The main uses of α_2-adrenoceptor agonists in veterinary medicine are to provide chemical restraint, anxiolysis and analgesia. They may be used seperately or in combination with other sedative/analgesics to allow veterinarians to carry out minor procedures such as suturing lacerations or radiography. Alternatively, they may be used for premedication before anesthesia with other drugs, where they facilitate compliance of the animal for presurgical preparation (e.g. clipping hair, placing an intravenous catheter) and reduce the doses of anesthetic drugs needed for induction and maintenance (Vickery et al. 1988; Hellebrekers & Sap 1997). The doses of α_2- agonists used for these purposes generally have significant effects on cardiovascular function, especially in dogs (Pypendop & Verstegen 1998; Sinclair et al. 2003). Thus it is generally advised that α_2-agonists should not be used in animals with compromised cardiovascular function. The increase in systemic vascular resistance associated with the potent α_2-agonists may be of particular concern in patients with mitral regurgitation or dilated cardiomyopathy (Pypendop & Verstegen 1998; Sinclair et al. 2003). Given these effects it is interesting to note that α_2-agonists are being used in human patients with coronary artery disease and that they are benefiting from such an approach (Mangano 1997; Wijeysundera et al. 2003); these drugs are associated with decreased likelihood of tachycardia, reduced response to stress (Flacke et al. 1987; Mangano 1997; Talke et al. 2000) and reduced mortality (Wijeysundera et al. 2003). The doses of α_2-agonists used in animals are larger than those used conventionally in human beings. With medetomidine, this difference may be partially attributed to the use of the less potent racemic mixture in animals, whereas the more potent dexmedetomidine isomer is usually used in human beings. If all the pharmacological activity resides in the dex isomer then this could account for the dose of racemic medetomidine being, at most, twice that of dexmedetomidine. However, in the dog it is common to use doses of medetomidine exceeding 10 $\mu g\ kg^{-1}$ whereas the doses of dexmedetomidine used in human patients are often $<1\ \mu g\ kg^{-1}$, i.e. more than a 10-fold difference in dose. This difference is greater than can be explained on the basis of allometric scaling. In dogs, medetomidine administered pre-operatively has been shown to reduce minimum alveolar concentration for inhalation (MAC) and peri-operative stress (Vickery et al. 1988; Weitz et al. 1991; Vaisanen et al. 2002) but low doses of dexmedetomidine have not been used intraoperatively.

Dexmedetomidine decreases the MAC of isoflurane in human patients when used as a continuous infusion (Aho et al. 1991). The objective of this study was to determine the change in the MAC of isoflurane in dogs with three doses of dexmedetomidine given as constant rate infusions following a loading dose for each infusion rate.

Materials and methods

Animals and study design

The project was approved by the Ethics Committee for Animal Experiments of the University of Helsinki.

Six Beagles weighing between 13.0 and 17.7 kg, and aged 6 years were used in the project. They were found to be healthy on physical examination and were housed in a group in a large room and received outdoor exercise daily. Commercial dog food was given twice daily, and water was freely available.

The dogs were anesthetized four times with isoflurane for determining minimum alveolar concentration that prevented movement in response to a supramaximal stimulus in 50% of the animals (MAC) (Eger et al. 1965). On each occasion they received one of the four treatments that were assigned in random order. The four treatments were: saline, low dose dexmedetomidine (loading dose 0.1 $\mu g\ kg^{-1}$ IV followed by an infusion of 0.1 $\mu g\ kg^{-1}\ hour^{-1}$), middle dose dexmedetomidine (loading dose 0.5 $\mu g\ kg^{-1}$ IV followed by an infusion of 0.5 $\mu g\ kg^{-1}\ hour^{-1}$), and high dose dexmedetomidine (loading dose 3 $\mu g\ kg^{-1}$ IV followed by an infusion of 3 $\mu g\ kg^{-1}\ hour^{-1}$). The dexmedetomidine was made up in a saline solution such that the same infusion volumes were used for all four treatments. The loading doses were calculated on the basis of the pharmacokinetics of dexmedetomidine (Kuusela et al. 2000) and the method described by Wagner (1974). At least 2 weeks were allowed between treatments.

Anesthesia

After placing a 20 SWG catheter (Optiva*2; Johnson & Johnson Medical, Brussels, Belgium) in a cephalic vein, anesthesia was induced using a mask and isoflurane delivered along with oxygen. Acetated