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RESEARCH PAPER

A comparison of the effects of two different doses of ketamine used for co-induction of anaesthesia with a target-controlled infusion of propofol in dogs

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Abstract

Objective To assess the cardiorespiratory and hypnotic-sparing effects of ketamine co-induction with target-controlled infusion of propofol in dogs.

Study design Prospective, randomized, blinded clinical study.

Animals Ninety healthy dogs (ASA grades I/II). Mean body mass 30.5 ± SD 8.6 kg and mean age 4.2 ± 2.6 years.

Methods All dogs received pre-anaesthetic medication with acepromazine (0.03 mg kg^{-1}) and morphine (0.2 mg kg^{-1}) administered intramuscularly 30 minutes prior to induction of anaesthesia. Heart rate and respiratory rate were recorded prior to premedication. Animals were allocated into three different groups: Group 1 (control) received 0.9% NaCl, group 2, 0.25 mg kg^{-1} ketamine and group 3, 0.5 mg kg^{-1} ketamine, intravenously 1 minute prior to induction of anaesthesia, which was accomplished using a propofol target-controlled infusion system. The target propofol concentration was gradually increased until endotracheal intubation was possible and the target concentration at intubation was recorded. Heart rate, respiratory rate and noninvasive blood pressure were recorded immediately prior to induction, at successful intubation and at 3 and 5 minutes post-intubation. The quality of induction was graded according to the amount of muscle twitching and paddling observed. Data were analysed using a combination of chi-squared tests, Fisher's exact tests, Kruskal–Wallis, and ANOVA with significance assumed at $p < 0.05$.

Results There were no significant differences between groups in the blood propofol targets required to achieve endotracheal intubation, nor with respect to heart rate, noninvasive blood pressure or quality of induction. Compared with the other groups, the incidence of post-induction apnoea was significantly higher in group 3, but despite this dogs in this group had higher respiratory rates overall.

Conclusions and clinical relevance Under the conditions of this study, ketamine does not seem to be a useful agent for co-induction of anaesthesia with propofol in dogs.

Keywords co-induction, dogs, ketamine, propofol, target-controlled infusion.

Introduction

Propofol is commonly administered for the induction of anaesthesia in dogs. Adverse effects include reduced arterial blood pressure and apnoea or hypoventilation (Smith et al. 1993). The mechanisms underlying the decrease in arterial pressure after propofol administration are believed to be inhibition of myocardial contractility and a decrease in systemic vascular resistance (Pagel & Warltier 1993; Wouters et al. 1995). Although usually tolerated well in healthy animals, these changes may lead to hypotension in hypovolaemic dogs (Ilkiw et al. 1992). Propofol causes hypoventilation by directly depressing central inspiratory drive and the ventilatory response to $PaCO_2$ (Jonsson et al. 2005). Post-induction cyanosis may be observed (Smith et al. 1993). Excitatory effects such as paddling, muscle twitching or opisthotonus have also frequently been reported after intravenous propofol administration (Davies 1991). Pre-anaesthetic medication can reduce the dose of propofol required to induce anaesthesia (Geel 1991; Sano et al. 2003), and diminishes, but does not eliminate the incidence of adverse effects (Smith et al. 1993).

A target-controlled infusion (TCI) comprises a portable computerized infusion system that allows a desired target blood concentration of propofol to be selected. Software consists of a pharmacokinetic model, a set of specific pharmacokinetic variables for propofol and infusion control algorithms. The patient's age and weight are entered into the device and the desired target blood concentration is selected. The TCI software then delivers a rapid infusion rate until the model predicts that the target concentration selected is achieved, and a variable rate infusion is then continued to maintain the set target concentration. A TCI system for delivering propofol in dogs has been developed and validated (Beths et al. 2001) and an induction target of 3.5 μg mL^{-1} has been shown to be optimal for successful induction of anaesthesia in pre-medicated dogs (Musk et al. 2005). In human studies, it has been demonstrated that there is less cardiovascular depression during induction with the TCI system when compared with manually controlled infusions (Chaudhri et al. 1992), presumably because it is easier to titrate the propofol concentration upwards.

The term 'co-induction' has been used to describe the practice of administering a sedative or other anaesthetic agent at the time of induction to decrease the dose of the primary hypnotic agent, with a view to reducing the incidence of agent-specific undesired effects, most notably, hypotension. The benzodiazepines and potent opioids are used for this purpose most commonly (Armein et al. 1995). However, midazolam did not reduce propofol requirements for induction of anaesthesia in pre-medicated dogs (Covey-Crump & Murison 2008). Alfentanil, when combined with propofol for induction of anaesthesia with a TCI system in dogs, reduced blood propofol targets, but resulted in lower mean arterial blood pressures (MAP) than propofol alone (Auckburally et al. 2008). Similarly fentanyl co-induction resulted in a reduced dose requirement of propofol but did not significantly alter cardiovascular parameters (Covey-Crump & Murison 2008).

Ketamine is a phencyclidine derivative. It is an *N*-methyl-D-aspartate receptor antagonist with analgesic and anaesthetic properties. Unlike many anaesthetics, ketamine usually causes an increase in heart rate and arterial blood pressure as a result of increased sympathetic efferent activity (Wong & Jenkins 1974). However, these cardiovascular effects may be unacceptable in some circumstances leading to the development of hypertension and tachycardia (Karapinar et al. 2006). Ketamine also has been associated with violent recoveries, muscle hypertonicity and convulsions in dogs (Haskins et al. 1985); therefore there may be a rationale for combining propofol with ketamine if the hypnosis and cardiovascular depression produced by propofol counterbalances the psychomimetic and cardiostimulatory effects of ketamine.

In human anaesthesia, the use of ketamine (0.3 mg kg^{-1}) in conjunction with propofol has been shown to reduce the dose of propofol required for induction of anaesthesia (Srivastava et al. 2006). It has also been reported that the co-administration of a low dose of ketamine with propofol for induction of anaesthesia attenuates any adverse haemodynamic or respiratory effects compared with propofol alone (Furuya et al. 2001; Srivastava et al. 2006). An additional advantage is that low dose ketamine (0.15 mg kg^{-1}) has been shown to reduce post-operative pain (Roytblat et al. 1993).

Propofol followed by ketamine (2 mg kg^{-1} each) has been compared with propofol alone (4 mg kg^{-1}) given as a bolus dose for induction of anaesthesia in dogs (Lerche et al. 2000). The combination of propofol and ketamine resulted in higher heart rates but no difference in arterial blood pressures between groups. However, to date, there are no