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RESEARCH PAPER

# Comparison of propofol with ketofol, a propofol-ketamine admixture, for induction of anaesthesia in healthy dogs

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## Abstract

**Objective** To compare anaesthetic induction in healthy dogs using propofol or ketofol (a propofol-ketamine mixture).

**Study design** Prospective, randomized, controlled, 'blinded' study.

**Animals** Seventy healthy dogs (33 males and 37 females), aged 6–157 months and weighing 4–48 kg.

**Methods** Following premedication, either propofol (10 mg $mL^{-1}$) or ketofol (9 mg propofol and 9 mg ketamine $mL^{-1}$) was titrated intravenously until laryngoscopy and tracheal intubation were possible. Pulse rate (PR), respiratory rate ($f_R$) and arterial blood pressure (ABP) were compared to post-premedication values and time to first breath (TTFB) recorded. Sedation quality, tracheal intubation and anaesthetic induction were scored by an observer who was unaware of treatment group. Mann–Whitney or *t*-tests were performed and significance set at $p \leq 0.05$.

**Results** Induction mixture volume (mean ± SD) was lower for ketofol (0.2 ± 0.1 mL $kg^{-1}$) than propofol (0.4 ± 0.1 mL $kg^{-1}$) ($p < 0.001$). PR increased following ketofol (by 35 ± 20 beats $minute^{-1}$) but not consistently following propofol (4 ± 16 beats $minute^{-1}$) ($p < 0.001$). Ketofol administration was associated with a higher mean arterial blood pressure (MAP) (82 ± 10 mmHg) than propofol (77 ± 11) ($p = 0.05$). TTFB was similar, but ketofol use resulted in a greater decrease in $f_R$ (median (range): ketofol −32 (−158 to 0) propofol −24 (−187 to 2) breaths $minute^{-1}$) ($p < 0.001$). Sedation was similar between groups. Tracheal intubation and induction qualities were better with ketofol than propofol ($p = 0.04$ and 0.02 respectively).

**Conclusion and clinical relevance** Induction of anaesthesia with ketofol resulted in higher PR and MAP than when propofol was used, but lower $f_R$. Quality of induction and tracheal intubation were consistently good with ketofol, but more variable when using propofol.

*Keywords* dog, induction of anaesthesia, ketamine, ketofol, propofol.

## Introduction

Propofol is widely used for induction of anaesthesia in dogs. It is a phenol-derivate sedative-hypnotic agent with rapid onset and short duration of action after a single bolus, which is followed by a smooth recovery. However, it is also associated with cardio-pulmonary depression (Short & Bufalari 1999), pain at induction [especially when micro-emulsion

formulations are used (Michou et al. 2012)], and excitation following induction of anaesthesia characterised by muscle twitching, panting, paddling, limb rigidity and opisthotonus (Davies & Hall 1991).

Ketamine is a phencyclidine derivate with sedative, anaesthetic and analgesic effects produced by N-methyl-D-aspartate receptor antagonism. The cardiovascular effects of ketamine are a direct depression of myocardial contractility (Pagel et al. 1992; Gelissen et al. 1996), usually masked by stimulation of sympathetic efferent activity, which increases heart rate and arterial blood pressure (Wong & Jenkins 1974).

Coadministration of ketamine and propofol, administered using separate syringes, has been successfully used with the intention of counteracting the unwanted effects of these drugs. In dogs, the decrease in heart rate occurring at anaesthetic induction was smaller when ketamine and propofol were administered (propofol and ketamine in separate syringes) than when propofol was given alone (Lerche & Nolan 2000) and similar findings were also observed in humans (Hui et al. 1995). Combining both drugs in a single syringe aims to simplify drug administration.

The mixture of propofol and a low dose of ketamine (ketofol) in the same syringe has been studied, particularly as continuous intravenous (IV) infusions for sedation and analgesia, both in healthy volunteers (Morse et al. 2003) and clinical patients in the emergency department (Willman & Andolfatto 2007; Andolfatto & Willman 2010; Phillips et al. 2010; Da Silva et al. 2011). The combination of these drugs sought the haemodynamic stability observed when given separately, with the convenience of managing only a single infusion. In addition to the clinical data reported, the physical and chemical stability of ketamine: propofol combinations in 1:1 and 3:7 (mg) ratios has been demonstrated (Donnelly et al. 2008). Ketofol has received interest in veterinary anaesthesia, especially in feline patients. Ravasio et al. (2012) documented the use of ketofol infusion for ovariectomy in cats and Zonca et al. (2012) reported the pharmacokinetics of ketofol in cats after induction of anaesthesia and 25 minute constant rate infusion. To date, there is no information regarding the use of 1:1 propofol/ketamine admixture in dogs for induction of anaesthesia and its haemodynamic characteristics.

This study aimed to compare the cardiorespiratory variables and induction characteristics of dogs anaesthetized with either propofol or a propofol-ketamine admixture.

## Materials and methods

The study was approved by the institutional ethics committee and the Veterinary Medicines Directorate (VMD) (animal test certificate number ATC-S-026), and informed owner consent was obtained.

Seventy dogs requiring general anaesthesia for various diagnostic and surgical procedures were included in the study. All the animals were assigned to American Society of Anesthesiologists (ASA) categories I or II on the basis of a thorough physical examination performed by the main investigator (FMT). Exclusion criteria were animals in ASA categories III to V, pregnant or lactating bitches, anaesthetic duration shorter than one hour and any case where it was felt the use of one or more of the drugs described in the protocol was contraindicated.

Dogs were fasted for 12 hours prior to induction of anaesthesia. Water was available until pre-anaesthetic medication was administered. This medication consisted of 0.02 mg $kg^{-1}$ acepromazine (ACP injection 2 mg $ml^{-1}$, Novartis Animal Health, UK) and 0.2 mg $kg^{-1}$ methadone (Physeptone injection, methadone 1%, Martindale Laboratories, UK) administered by a single intramuscular injection in the lumbar epaxial muscles.

Thirty minutes after premedication, sedation was scored using a four point scale (0 = no sedation to 3 = profound sedation) as described by Murison (2001) (Appendix S1). An 18 or 20 gauge catheter (Jelco, Smith Medical International Ltd., UK) was inserted into a cephalic vein. A suitable blood pressure cuff (Critikon Soft-cuf, GE Healthcare, UK) (cuff width/metatarsal circumference ratio of 0.4) was placed over the dorsopedal artery for oscillometric blood pressure monitoring (Beneview T5, Shenzhen Mindray Bio-Medical Electronics Co, China). The arterial blood pressure was measured 1, 3 and 5 minutes after catheter placement. At these time points, pulse rate (PR) and breathing rate ($f_R$) were also recorded.

Dogs were randomly allocated to receive either propofol (Propoflo, Abbott, UK) or ketofol (1:1 mixture of approximately 9 mg $mL^{-1}$ propofol and 9 mg $mL^{-1}$ ketamine). This admixture was made by aseptically adding 200 mg of ketamine (Narketan 10, Vetoquinol, UK) to a 200 mg vial of propofol (Propoflo, Abbott, UK). Each vial of ketofol was kept for a maximum of 12 hours. A volume equivalent to