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SHORT COMMUNICATION

Chronotropic effect of propofol or alfaxalone following fentanyl administration in healthy dogs

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Abstract

Objective To compare the effect of alfaxalone and propofol on heart rate (HR) and blood pressure (BP) after fentanyl administration in healthy dogs.

Study design Prospective, randomised clinical study.

Animals Fifty healthy client owned dogs (ASA I/II) requiring general anaesthesia for elective magnetic resonance imaging for neurological conditions.

Methods All dogs received fentanyl 7 μg kg^{-1} IV and were allocated randomly to receive either alfaxalone ($n = 25$) or propofol ($n = 25$) to effect until endotracheal (ET) intubation was possible. Heart rate and oscillometric BP were measured before fentanyl (baseline), after fentanyl (Time F) and after ET intubation (Time GA). Post-induction apnoea were recorded. Data were analysed using Fisher's exact test, Mann Whitney *U* test and one-way ANOVA for repeated measures as appropriate; p value <0.05 was considered significant.

Results Dogs receiving propofol showed a greater decrease in HR (−14 beat $minute^{-1}$, range −47 to 10) compared to alfaxalone (1 beat $minute^{-1}$, range −33 to 26) ($p = 0.0116$). Blood pressure decreased over the three time periods with no difference between groups. Incidence of post-induction apnoea was not different between groups.

Conclusion Following fentanyl administration, anaesthetic induction with propofol resulted in a greater negative chronotropic effect while alfaxalone preserved or increased HR.

Clinical relevance Following fentanyl administration, HR decreases more frequently when propofol rather than alfaxalone is used as induction agent. However, given the high individual variability and the small change in predicted HR (−7.7 beats per minute after propofol), the clinical impact arising from choosing propofol or alfaxalone is likely to be small in healthy animals. Further studies in dogs with myocardial disease and altered haemodynamics are warranted.

Keywords alfaxalone, dogs, fentanyl, heart rate, propofol.

Introduction

Fentanyl often is used as co-induction agent to decrease the requirement of injectable anaesthetic and attenuate the hypertensive response to endotracheal (ET) intubation in humans (Billard et al. 1994). In dogs, fentanyl can cause bradycardia and hypotension as well as respiratory depression especially when it is combined with anaesthetic agents (Nolan & Reid 1991). Similarly, the combination of fentanyl – propofol caused hypotension and reduction in heart rate (HR) prior to ET intubation in humans (Billard et al. 1994).

Propofol and alfaxalone are commonly used to induce anaesthesia in dogs. Propofol and alfaxalone affected HR differently in dogs sedated with acepromazine and pethidine (Amengual et al. 2013). However, in their study, because HR was different

between groups following premedication, the effect of anaesthetic induction agent could not be determined with certainty. According to Covey-Crump & Murison (2008), the association between fentanyl (2 μg kg^{-1}) and propofol did not result in statistically significant negative chronotropic effect compared to propofol alone in dogs sedated with acepromazine and morphine. To the authors' knowledge, there are no publications investigating the cardiovascular effects of fentanyl – alfaxalone combination in dogs.

Our clinical experience suggested that administration of alfaxalone after fentanyl results in less bradycardia compared to propofol in dogs. The study objective was to compare the change in HR and blood pressure (BP) after propofol and alfaxalone following fentanyl premedication in healthy dogs. We hypothesised that alfaxalone would result in either preservation or increase in HR compared to that of propofol.

Materials and methods

Animals

Fifty client-owned dogs scheduled to undergo magnetic resonance imaging (MRI) to investigate neurological conditions were recruited. Dogs were excluded if: 1) body weight was less than 10 kg; 2) physical status according to the American Society of Anesthesiology (ASA) was greater than II; 3) cardiovascular disease was present; 4) raised intracranial pressure was suspected; 5) drugs affecting BP and/or baroreceptor response had been administered; 6) temperament precluded placement of an intravenous (IV) catheter without sedation; 7) adverse reactions to at least one of the drugs used in the study had been reported.

The study protocol was registered with the Veterinary Medicines Directorate (SI 2011/2159) following approval by Dick White Referrals local ethical committee. Informed written owner consent was obtained prior to enrolment.

Study design

Following hospital admission all dogs were weighed and an IV catheter was placed in the cephalic vein. The study was conducted on the day of admission in most dogs. If the dog was hospitalised overnight prior to the study, food was withheld for at least eight hours, while access to water was allowed *ad libitum*.

Sample size calculations suggested that 20 dogs per group were necessary to detect a difference of 10 beats per minute in HR, with a standard deviation (SD) of 12 beats per minute, $\alpha = 0.05$ and $\beta = 0.2$ (G*Power, version 3.1.3). The number of animals enrolled in the study was increased to 25 per group in order to compensate for lost data.

Dogs were allocated randomly, using a computer generated randomisation table (www.random.org), to receive propofol (PropoFlo Plus; Abbott, UK) [Group P] or alfaxalone (Alfaxan; Vétoquinol, UK) [Group A] to induce anaesthesia, in both cases after administration of fentanyl (Sublimaze; Janssen-Cilag, UK) 7 μg kg^{-1} IV (see below for time schedule). Heart rate and oscillometric BP were measured before fentanyl administration (baseline), after fentanyl administration (Time F), and after ET intubation (Time GA). In each occasion, a multiparametric monitor (PM8000 or MEC1200; Mindray, UK) automatically measured BP and simultaneously averaged HR at one minute intervals; displayed data were subsequently transcribed in a Microsoft Excel spreadsheet. Heart rate was derived from a lead II electrocardiogram, while BP was measured using a cuff (width approximately 40% of limb circumference) placed either just above the carpal joint or on the metatarsus. Three BP measurements were obtained, and at least two additional readings were made if mean arterial pressures (MAP) variability was greater than 10%. When possible, dogs were kept in sternal or right lateral recumbency with minimal restraint used if necessary. Oxygen (100 mL kg^{-1} $minute^{-1}$) was supplemented during the study period through the end of the anaesthetic breathing system which was placed near the nose.

After baseline data collection, fentanyl was administered IV over 30 seconds. One minute later, HR and BP measurements were obtained (Time F). Time between fentanyl administration and induction of general anaesthesia (GA) was recorded. Anaesthesia was induced after measurements at Time F were obtained, using either propofol or alfaxalone administered slowly to effect. Ventral rotation of the eye and jaw muscle relaxation were used as endpoints to attempt ET intubation. If ET intubation was not possible at the first attempt, additional anaesthetic agent was administered at the discretion of the anaesthetist, and the total dose recorded. Following ET intubation, HR and BP measurements were repeated as previously described (Time GA). The ET tube was connected to a rebreathing system and isoflurane vaporiser set at

