

RESEARCH PAPER

Sedative, cardiovascular, haematologic and biochemical effects of four different drug combinations administered intramuscularly in cats

Kirsten Biermann, Stephan Hungerbühler, Reinhard Mischke & Sabine BR Kästner

Small Animal Clinic, University of Veterinary Medicine Hannover, Foundation, Hannover, Germany

Correspondence: Kirsten Biermann, Small Animal Clinic, University of Veterinary Medicine Hannover, Bünteweg 9, D-30559 Hannover, Germany. E-mail: kirsten.biermann@tiho-hannover.de

Abstract

Objective To compare effects of four drug combinations on sedation, echocardiographic, haematologic and biochemical variables and recovery in cats.

Study design Experimental randomized 'blinded' cross-over study.

Animals Six healthy cats.

Materials and Methods Treatments were administered intramuscularly: midazolam 0.4 mg kg⁻¹ and butorphanol 0.4 mg kg⁻¹ (MB); midazolam 0.4 mg kg⁻¹, butorphanol 0.4 mg kg⁻¹ and ketamine 3 mg kg⁻¹ (MBK); midazolam 0.4 mg kg⁻¹, butorphanol 0.4 mg kg⁻¹ and dexmedetomidine 5 µg kg⁻¹ (MBD); ketamine 3 mg kg⁻¹ and dexmedetomidine 5 µg kg⁻¹ (KD). Sedation was evaluated at time-points over 10 minutes post injection. Echocardiography, systolic arterial blood pressure (SAP) measurement and blood sampling were performed at baseline and from 10 minutes after treatment. Quality of recovery was scored. Data were analysed by ANOVA for repeated measures. $p < 0.05$ was considered significant.

Results The lowest sedation score was obtained by MB, (median 10.5 [7; 20]), highest by KD (36.5 [32; 38]). Quality of recovery was best with KD (0.5 [0; 2]), and worst with MB (7.5 [4; 11]). Relative to baseline measurements, treatments decreased SAP

by 17%, 25%, 13%, 5% in MB, MBK, MBD and KD, respectively. Heart rate decreased ($p < 0.05$) after MBD (44%) and KD (34%). All treatments decreased stroke volume by 24%, 21%, 24%, 36%, and cardiac output by 23%, 34%, 54%, 53% in MB, MBK, MBD and KD, respectively. Packed cell volume was decreased ($p < 0.05$) by 20%, 31%, 29% in MBK, MBD and KD, respectively. Plasma glucose was increased after MBD (31%) and KD (52%) and lactate concentration was decreased ($p < 0.05$) after MBK (58%), MBD (72%) and KD (65%).

Conclusions and clinical relevance The MB combination did not produce sedation in healthy cats. Treatment MBK led to acceptable sedation and minimal cardiovascular changes. Both treatments with dexmedetomidine produced excellent sedation and recovery but induced more cardiovascular depression and haematologic changes.

Keywords butorphanol, dexmedetomidine, echocardiography, feline, ketamine, midazolam.

Introduction

As a species, cats can be difficult to handle for diagnostic procedures in veterinary practice, and therefore sedation is required often in order to perform common diagnostic procedures such as echocardiography or blood sampling (Moffat 2008). In order to produce diagnostically useful results, drug combinations used to facilitate blood sampling

and echocardiography should have minimal cardiovascular effects and minimal effects on haematological variables. Many combinations of sedative drugs have been used and described for feline sedation; popular drug combinations include midazolam, ketamine, butorphanol and an alpha-2 agonist, of which dexmedetomidine is that most recently licensed for administration to cats.

Midazolam is a water-soluble benzodiazepine with a rapid onset of action after intramuscular (IM) injection. Administered alone, it can cause ataxia and dysphoria in cats, thus making restraint and handling more difficult (Ilkiw et al. 1996). Previous authors reported minimal cardiovascular depression in cats sedated with a midazolam-ketamine combination (Akkerdaas et al. 2001).

Butorphanol is a synthetic morphine derivative with agonistic effects at the κ -opioid receptors and partial agonist and antagonist activity at the μ -opioid receptors (Commiskey et al. 2005). In cats, butorphanol provides visceral analgesia and leads to a mild sedation when administered alone (Ansah et al. 2002).

Ketamine is absorbed rapidly after IM administration (Hanna et al. 1988), has a short onset of action and produces a dissociative state including analgesia and amnesia (Kohrs & Durieux 1998). As a result of sympathetic stimulation it often produces significant increases in heart rate, cardiac output and blood pressure in healthy cats (Child et al. 1972). However, it has a direct negative inotropic effect on the myocardium, and cardiovascular effects may vary depending upon the patients condition and co-administered drugs (Clanachan et al. 1976).

Dexmedetomidine, an alpha₂-adrenoceptor agonist (α_2 -agonist), is the active enantiomer of racemic medetomidine (Virtanen et al. 1988). Dexmedetomidine induces dose-dependent sedation, analgesia and muscle relaxation in cats (Ansah et al. 1998) with marked decreases in heart rate, cardiac output, and transient changes in blood pressure (Selmi et al. 2003). Furthermore, dexmedetomidine can cause a decrease in respiratory rate and body temperature (Granholm et al. 2006).

Many IM drug combinations for sedation and short term anaesthesia have been investigated in cats previously but, to our knowledge, the effects on diagnostic echocardiography, haematologic and biochemical variables have not been thoroughly evaluated. The aim of this study was to compare the effects of midazolam and butorphanol alone or

combined with, either ketamine or dexmedetomidine and ketamine combined with dexmedetomidine on quality of sedation, echocardiographic, haematologic and biochemical variables and recovery in cats.

Materials and methods

The experiments were performed with the approval of the Ethical Committee of the Lower Saxony State Office for Consumer Protection and Food Safety (33.9-42502-04-08/1471).

Animals

Six adult domestic short-hair cats, three neutered males and three females (one neutered), weighing 4.29 ± 1.00 kg (mean \pm SD) [range 3.00–6.00 kg] and aged 10.3 ± 4.3 years were the subject of the experiment. Animals were group-housed, given free access to water and were provided with commercially available cat food (Feline Health Nutrition, Royal Canin Tiernahrung GmbH & Co., KG, Germany). Health status was assessed by means of physical examination, echocardiographic examination, a complete blood count and serum biochemical analyses. All cats were considered healthy based on published reference ranges (Ettinger & Feldman 2010; Rizzi et al. 2010).

Experimental design

The study was carried out as a randomised cross-over experimental trial, with the main investigator unaware of the treatment used. A period of eight days was allowed between treatments to avoid residual drug effects. Food but not water was withheld for eight hours prior to treatment. On the day of experiment each cat was weighed and underwent a physical examination. Both conscious and sedated cats were restrained in lateral recumbency for echocardiography and in sternal recumbency for SAP measurement. The chronological order of the experimental procedures is given in Fig. 1. Baseline measurements were taken of all echocardiographic variables, blood samples SAP and rectal temperature. Each cat then received one of the four treatments. Sedation was scored over the first 10 minutes. At 10 minutes after injection echocardiography was repeated, followed by SAP measurement and blood sampling. Measurements were complete approximately 45 minutes after drug

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