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RESEARCH PAPER

Development of a sedation protocol using orally administered tiletamine–zolazepam–acepromazine in free-roaming dogs

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Abstract

Objective To investigate the sedative effects in dogs of tiletamine–zolazepam–acepromazine (TZA) or ketamine–flunitrazepam (KF) administered orally and to evaluate the effectiveness of encapsulated TZA for capturing free-roaming dogs.

Study design Experimental study followed by a field trial.

Animals Six research dogs and 27 free-roaming dogs.

Methods In a pilot study, six research dogs were administered liquid TZA (20 mg kg^{-1} tiletamine–zolazepam and 2 mg kg^{-1} acepromazine) or liquid KF (50 mg kg^{-1} ketamine and 2 mg kg^{-1} flunitrazepam) orally: treatment 1, forcefully squirting liquid medication into the mouth; treatment 2, encapsulating liquid medication for administration in canned food; treatment 3, administering liquid medication mixed with gravy. Sedation was scored. A follow-up field trial attempted capture of 27 free-roaming dogs.

Results In the pilot study, the median time (range) to lateral recumbency (% dogs) after TZA administration was as follows: treatment 1, 47.5 (35–80) minutes (67%); treatment 2, 30 (15–65) minutes (83%); and treatment 3, 75 (45–110) minutes (100%). No dogs in KF treatment 2 or 3 achieved lateral recumbency. Based on these results, 20 free-roaming dogs were offered encapsulated TZA in canned food: TZ (20 mg kg^{-1}) and acepromazine (2 mg kg^{-1}). Of these, no further drugs to four dogs (one dog captured), 10 dogs were administered a second dose within 30 minutes (five dogs captured) and six dogs were administered TZ (5 mg kg^{-1}) and xylazine (1.1–2.2 mg kg^{-1}) intramuscularly by blow dart (six dogs captured). Seven dogs were initially offered twice the TZA dose (five dogs captured). In total, 63% free-roaming dogs were captured after administration of encapsulated TZA in canned food.

Conclusions and clinical relevance Oral administration of encapsulated TZA in canned dog food can aid in the capture of free-roaming dogs, but additional drugs may be required. The sedation onset time and medication palatability influenced the capture rate.

Keywords acepromazine, dogs, flunitrazepam, ketamine, sedation, tiletamine–zolazepam.

Introduction

Veterinarians and welfare groups sedate or anesthetize free-roaming dogs to facilitate capture for medical treatment or for transportation to shelters or veterinary clinics for medical and surgical procedures, such as ovariohysterectomy, castration and treatment of traumatic injuries. Blowguns have been used to perform intramuscular (IM) injections in wild animals (Váhala 1993; Sontakke et al. 2009). In the authors' experience, however, free-roaming dogs successfully administered IM injection of drugs using this technique frequently escape from the operator's

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sight before achieving adequate sedation for safe handling. Furthermore, even when sedated, these dogs may maintain a considerable distance from the operator, confounding capture. In some situations, feral dogs that can be approached may be captured in nets.

Sedative and anesthetic drugs may be administered orally, either by ingestion (oral) or oral transmucosal (OTM) routes, and both routes may be involved in some cases, e.g. spraying the drug into the animal's mouth (Ramsay & Wetzel 1998; Wetzel & Ramsay 1998; Grove & Ramsay 2000; Kearns et al. 2000). However, after absorption from the gastrointestinal tract, the medication is immediately metabolized by the liver, affecting its bioavailability (Page & Maddison 2008). The bioavailability of ketamine administered through an IM injection is 93% in humans, but decreases to 32% following sublingual administration, and further decreases to 16% following oral administration (Grant et al. 1981; Clements et al. 1982; Chong et al. 2006). OTM administration of detomidine in animals has shown inconsistent results, ranging from minimal sedation efficacy to an efficacy equal to that of IM injection with the same dose (Malone & Clarke 1993; Karaaslan et al. 2006; Slingsby et al. 2009; Hokkanen et al. 2014).

Winterborn et al (2008) reported that in rhesus macaques (*Macaca mulatta*), administering a juice combined with either ketamine alone or ketamine in combination with medetomidine did not produce sufficient sedation for safe handling. Nevertheless, the day after this insufficient sedation, all of the animals approached and drank the juice from a syringe. This observation suggests that an oral administration has the potential to be repeatedly used. A combination of tiletamine–zolazepam–acepromazine (TZA) or pentobarbital sodium alone via oral ingestion with food consistently induces profound sedation in dogs (Ramsay & Wetzel 1998). In addition, Wetzel & Ramsay (1998) reported that OTM administration of a combination of detomidine and ketamine is an effective and reliable method for sedating cats.

The aims of the present study were to 1) evaluate the sedative efficacy of an oral administration of TZA or ketamine–flunitrazepam (KF) in research dogs; and based on the results, to 2) evaluate the effectiveness of oral TZA dosages for capture of free-roaming dogs. We hypothesized that different oral forms of TZA or KF administration can affect sedation efficacy in dogs, and that oral administration of TZA can be used in the capture of free-roaming dogs.

Materials and methods

The protocol for this project was approved by the Institutional Animal Care and Use Committee, National Chiayi University, Taiwan.

Research dogs

Six mixed-breed intact male dogs, weighing (mean ± standard deviation) 11.7 ± 4.3 kg and aged 4.3 ± 0.9 years, were selected. These dogs had been acquired from a humane shelter in accordance with local regulations, and were acclimated to the institutional facilities and personnel for at least 2 months. The dogs were considered to be healthy based on a physical examination and results of blood tests (complete blood count and serum biochemical examination). The dogs were housed separately in cages before and during the study. Food was withheld for 12–14 hours and water was available *ad libitum* before administration of medication.

All dogs were nonrandomly administered six treatments separated by 2 week intervals. The two drug combinations were either TZA consisting of tiletamine–zolazepam (20 mg kg^{-1}; 50 mg mL^{-1}; Virbac Laboratories, France) and acepromazine (2 mg kg^{-1}; 50 mg mL^{-1}; RX Veterinary Products, OH, USA), or KF consisting of flunitrazepam (2 mg kg^{-1}; 50 mg $tablet^{-1}$; Panbiotic Laboratories, Taiwan) dissolved in ketamine (50 mg kg^{-1}; 50 mg mL^{-1}; Pfizer Animal Health, Taiwan). Each drug combination was prepared in a liquid form and by encapsulation of the liquid in gelatin capsules (Fan Daming Co., Taiwan) by the investigators. TZA or KF were administered by different techniques on three occasions each: treatment 1, direct stream of liquid drug from a 10 mL syringe into the dog's buccal pouch, a treatment designed for predominant absorption through the oral mucosa; treatment 2, gelatin capsules containing the drug dose added to 100 g canned food (PurePetfood, Young Li Ltd., Taiwan), a treatment designed for absorption predominantly through the gastric or intestinal mucosa; and treatment 3, liquid drug mixed with 100 g of pork gravy, a treatment designed for partial absorption both oral transmucosally and the gastric or intestinal mucosa. The degree of sedation was scored every 5 minutes up to 120 minutes after medication administration. Time 0 was defined as the time of

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