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RESEARCH PAPER

Intramuscular injection of alfaxalone in combination with butorphanol for sedation in cats

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Abstract

Objective To assess quality of sedation following intramuscular (IM) injection of two doses of alfaxalone in combination with butorphanol in cats.

Study design Prospective randomized blinded clinical study.

Animals A total of 38 cats undergoing diagnostic imaging or noninvasive procedures.

Methods Cats were randomly allocated to receive butorphanol 0.2 mg kg^{-1} combined with alfaxalone 2 mg kg^{-1} (group AB2) or 5 mg kg^{-1} (group AB5) IM. If sedation was inadequate, alfaxalone 2 mg kg^{-1} IM was administered and cats were excluded from further analysis. Temperament [1 (friendly) to 5 (aggressive)], response to injection, sedation score at 2, 6, 8, 15, 20, 30, 40, 50 and 60 minutes, overall sedation quality scored after data collection [1 (excellent) to 4 (inadequate)] and recovery quality were assessed. Heart rate (HR), respiratory rate (f_R) and arterial haemoglobin saturation (SpO_2) were recorded every 5 minutes. Groups were compared using *t* tests and Mann–Whitney *U* tests. Sedation was analysed using two-way ANOVA, and additional alfaxalone using Fisher's exact test ($p < 0.05$).

Results Groups were similar for sex, age, body mass and response to injection. Temperament score was lower in group AB2 [2 (1–3)] compared to AB5 [3 (1–5)] ($p = 0.006$). Group AB5 had better sedation at 6, 8, 20 and 30 minutes and overall sedation quality was better in AB5 [1 (1–3)], compared to AB2 [3 (1–4)] ($p = 0.0001$). Additional alfaxalone was required for 11 cats in AB2 and two in AB5 ($p = 0.005$). Recovery quality, HR, f_R and SpO_2 were similar. Seven cats required oxygen supplementation. Complete recovery times were shorter in AB2 (81.8 ± 24.3 *versus* 126.6 ± 33.3 minutes; $p = 0.009$). Twitching was the most common adverse event.

Conclusions and clinical relevance In combination with butorphanol, IM alfaxalone at 5 mg kg^{-1} provided better quality sedation than 2 mg kg^{-1}. Monitoring of SpO_2 is recommended.

Keywords alfaxalone, butorphanol, cats, intramuscular, sedation.

Introduction

In cats, sedation is often required to enable diagnostic and other procedures to be performed. Intramuscular (IM) administration of sedative drugs may be preferred because intravenous (IV) administration may not always be possible due to the temperament of the cat, and subcutaneous (SC) administration of sedatives may result in long onset times and erratic absorption. Such sedation is often achieved using a combination of an opioid with an α-2 adrenoceptor agonist, with or without ketamine. Acepromazine or benzodiazepines may be used in combination with the aforementioned drugs. However, some of these agents might not be suitable for all patients due to their cardiorespiratory effects (Jacobs & Knight 1985; Harrison et al. 2011; Biermann et al. 2012). Other side effects, such as dysphoria, agitation (Biermann et al. 2012), vomiting (Harrison et al. 2011; Nagore et al. 2013), and decreased renal excretion in patients with renal insufficiency (Chang & Glazko 1974) may be undesirable.

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Alfaxalone, a synthetic neurosteroid solubilized in 2-hydroxypropyl-β-cyclodextrin, is licensed for induction and maintenance of anaesthesia in cats and dogs in several countries as Alfaxan. In Australia, New Zealand and South Africa, Alfaxan is licensed to provide sedation in cats IM at doses of 5−10 mg kg^{-1}. Although alfaxalone solubilized in Cremophor EL in combination with alphadolone (historically marketed as Saffan) was used by IM injection in cats (Haskins et al. 1975), no known studies have been published using Alfaxan in cats by IM injection when this project began.

Alfaxalone 5 mg kg^{-1} represents the lower dose recommended by the Australian data sheet for IM administration. At our clinic, even lower doses of alfaxalone are used IM and therefore 2 mg kg^{-1} of alfaxalone was chosen for comparison. Butorphanol, a synthetic opioid, which is licensed in the UK to provide sedation in cats in combination with medetomidine and/or ketamine, was chosen to be administered together with alfaxalone. Doses of 0.4 mg kg^{-1} are suggested for IM administration, but lower doses are commonly used clinically.

The aim of the study was to establish whether IM administration of alfaxalone at the recommended dose of 5 mg kg^{-1} or at a lower dose of 2 mg kg^{-1} would provide adequate sedation in cats undergoing diagnostic imaging or minor, noninvasive procedures, alone or in combination with butorphanol.

Material and methods

The study was approved by the Animal Health Trust Clinical Research Ethics Committee (AHT 03_09) and the Veterinary Medicines Directorate (ATC-S 007). Client-owned cats were enrolled in this prospective, randomized trial after informed and written owner consent was obtained. Cats, classified according to the American Association of Anesthesiologists physical status grading system as 1 or 2, requiring sedation for obtaining vascular access, diagnostic imaging or minor, noninvasive procedures were enrolled in the study. Exclusion criteria were concurrent treatment with phenobarbitone, benzodiazepines or opioids.

Each cat was randomly assigned to one of four treatment groups using a computer-generated randomization system. Cats received alfaxalone (Alfaxan; Jurox UK Ltd., UK) 2 mg kg^{-1} (group A2), alfaxalone 5 mg kg^{-1} (group A5) or butorphanol (Alvegesic; Dechra Veterinary Products Limited, UK) 0.2 mg kg^{-1} combined with alfaxalone 2 mg kg^{-1} (group AB2) or alfaxalone 5 mg kg^{-1} (group AB5).

Two investigators, similarly trained and experienced, who were unaware of treatment group, performed all scoring. The first six cats enrolled in the study were assessed by one investigator, then subsequent cats by the other.

Prior to drug administration, cats underwent a full clinical examination and a temperament score ranging from 1 (very friendly) to 5 (very aggressive) was assigned (Table S1). The drug combination was injected by a qualified veterinary nurse into the quadriceps muscle using a 2.5-mL syringe and a 25-gauge needle, with the volume varying depending on the body mass of the cat. The response to the injection ranging from 0 (none) to 4 (prolonged reaction) (Table S1) and time to onset of lateral recumbency were recorded. The sedation was scored at 2, 4, 6, 8, 15, 20, 30, 40, 50 and 60 minutes after drug administration using a multidimensional scoring system adapted from Young et al. (1990) (Table S2). Posture, resistance to maintenance of lateral recumbency, degree of muscular relaxation and response to a noise stimulus, (a click of the investigator's tongue 1 m away from the cat's head), were evaluated. A maximum score of 13 was possible, representing profound sedation. The procedure was started once the multidimensional sedation score was > 5. If after 12 minutes the score was < 5 or the procedure could not be completed due to inadequate sedation, an additional dose of alfaxalone 2 mg kg^{-1} was administered IM into the quadriceps muscle and any further recording excluded from data analysis apart from adverse events. If sedation remained inadequate 10 minutes later, the cat was removed from the study and alternative sedatives were administered. A blanket, with or without a heat pad, was used during the procedure at the discretion of the attending nurse. At the end of the procedure or before administering additional alfaxalone an overall sedation score ranging from 1 (excellent) to 4 (inadequate) was assigned to assess the quality of sedation (Table S1). Procedure time and rectal temperature were recorded before recovering the cat in an incubator or a kennel. Recovery was filmed and the time from first injection until sternal recumbency, standing and full recovery (walking without ataxia) were recorded. Recovery quality ranging from 1 (excellent) to 3 (poor) was scored (Table S1). The occurrence of side effects (head bobbing, opisthotonus, muscle twitching, exaggerated response to noise or touch, salivating or rubbing the face with the paws) was recorded. Heart rate (HR), respiratory rate (f_R) and arterial haemoglobin saturation (SpO_2;

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