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RESEARCH PAPER

Evaluation of butorphanol, medetomidine and midazolam as a reversible narcotic combination in free-ranging African lions (*Panthera leo*)

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Abstract

Objective To evaluate the effects of the combination butorphanol, medetomidine and midazolam (BMM) and its reversibility in lions.

Study design Prospective clinical trial.

Animals Thirty free-ranging lions, 10 male and 20 female, weighing 81–210 kg.

Methods Lions were immobilised with butorphanol mean 0.31 ± SD 0.034 mg kg^{-1}, medetomidine 0.052 ± 0.006 mg kg^{-1}, midazolam 0.21 ± 0.024 mg kg^{-1} and hyaluronidase 1250 IU administered intramuscularly with a dart gun. Upon recumbency, physiological parameters and anaesthetic depth were monitored 10–15 minutes after darting (T1) and repeated every 10 minutes for a further 30 minutes (T2, T3, T4). Arterial blood gas analyses were performed at T1 and T4. At the end of the procedure, 45–60 minutes after initial darting, immobilisation was reversed with naltrexone 0.68 ± 0.082 mg kg^{-1}, atipamezole 0.26 ± 0.031 mg kg^{-1}, and flumazenil 0.0032 ± 0.0007 mg kg^{-1} administered intravenously and subcutaneously.

Results The BMM combination rapidly induced immobilisation and lateral recumbency was reached within 7.25 ± 2.3 minutes. Median induction score [scored 1 (excellent) to 4 (poor)] was 1.4 (range 1–2). Cardio-respiratory parameters were stable. Heart rate varied from 32 to 72 beats per minute, respiratory rate from 14 to 32 breaths $minute^{-1}$ and rectal temperature from 36.6 to 40.3 °C. No sudden arousals were observed. Arterial blood gas analyses revealed a mean pH of 7.33, $PaCO_2$ of 33 mmHg and PaO_2 of 87 mmHg. Mild to moderate hypoxemia was seen in four lions. Recovery was smooth and lions were walking within 4.4 ± 4.25 minutes. Median recovery score [scored 1 (excellent) to 4 (poor)] was 1.3 (range 1–2).

Conclusion and clinical relevance The drug combination proved to be effective in immobilising free-ranging healthy lions of both sexes with minimal cardio-respiratory changes.

Keywords atipamezole, butorphanol, flumazenil, lion, medetomidine, midazolam, naltrexone.

Introduction

Safe and reliable immobilisation of African lions (*Panthera leo*) is an important tool for conservation-based programmes of free-ranging animals. Lions are anaesthetized routinely for sample collection, disease surveillance, research studies and treatment

(Herbst et al. 1985; Fahlman et al. 2005; Jacquier et al. 2006). Ideally, drugs used for the capture of free-ranging animals should induce immobilisation rapidly and reliably, provide stable cardio-respiratory function, and be fully reversible. Darted lions can be difficult to locate following a prolonged induction, especially if working in dense bush or at night, and they are vulnerable to unfavourable environmental conditions, injury or attack from other lions and predators during both the induction and recovery periods. The use of immobilising drug combinations which can be antagonised facilitates the management of adverse drug responses.

Various drugs and drug combinations have been used both in free-ranging and captive lions. In the 1970s, lions were immobilised using phencyclidine hydrochloride which tended to cause convulsions and resulted in very prolonged recovery periods (Bush et al. 1978). More recently, ketamine, often in combination with xylazine or medetomidine, has been used for the purpose, especially for lions held in captivity. Sudden recoveries without warning, bradycardia, vomiting and large dart volumes are drawbacks seen with these combinations (Herbst et al. 1985; Stander & Morkel 1991; Tomizawa et al. 1997; Quandt 2005). Tiletamine-zolazepam has been used for the immobilisation of free-ranging lions but, used alone, can cause prolonged and uncoordinated inductions and recoveries (King et al. 1977; Stander & Morkel 1991). When medetomidine is combined with tiletamine/zolazepam, the duration of immobilisation can be shortened and induction is smoother (Fahlman et al. 2005; Jacquier et al. 2006).

Combinations of medetomidine 0.01–0.05 mg kg^{-1}, butorphanol 0.1–0.4 mg kg^{-1} and midazolam or diazepam 0.15–1 mg kg^{-1} have been used successfully to immobilise domestic and exotic carnivore species, such as red wolf (*Canis rufus*), African wild dog (*Lycaon pictus*), cheetah (*Acinonyx jubatus*) and California sea lion (*Zalophus californianus*) (Verstegen & Petcho 1993; Larsen et al. 2002; Kalema-Zikusoka et al. 2003; Williams et al. 2003; Spelman 2004; Lafortune et al. 2005; Fleming et al. 2006). These combinations provided stable anaesthesia with good analgesia and muscle relaxation lasting for at least 40 minutes. Side effects included bradycardia, hypertension, hypoventilation, hypoxaemia, hypo- and hyperthermia and metabolic acidosis (Pypendop et al. 1996; Pypendop & Verstegen 1999; Larsen et al. 2002; Kalema-Zikusoka et al. 2003). Reversal of anaesthesia was rapid using either atipamezole alone or in combination with flumazenil and naltrexone or naloxone (Verstegen & Petcho 1993; Williams et al. 2003; Spelman 2004; Lafortune et al. 2005; Fleming et al. 2006). These results suggest that this combination would be applicable in larger carnivores, including lions.

The aim of this study was to evaluate the effects of the combination butorphanol, medetomidine and midazolam (BMM) and its reversibility using naltrexone, atipamezole and flumazenil in free-ranging lions.

Material and methods

The project was approved by Scientific Services of South African National Parks and complied with the Animal Use and Care Committee approved standard operating procedure (SOP) for the ''Capture, transportation and maintenance in holding facilities of wildlife''.

Twelve male and 21 female African lions were immobilised in order to test for bovine tuberculosis (*Mycobacterium bovis*) and to collect blood and tissue samples in Kruger National Park, South Africa. One female and two male animals were excluded from the study due to poor dart placement resulting in subcutaneous drug delivery. All individuals were considered healthy based on physical examination during immobilisation. The lions were attracted to a capture site in the evening using a zebra carcass as bait and playing a tape-recording of hyenas feeding at a kill as described previously (Smuts et al. 1977; McKenzie & Burroughs 1993). When a suitable lion was sighted, its body mass was estimated and a 3-mL dart (Dan-Inject International, South Africa) prepared. The intent was to administer medetomidine 0.05 mg kg^{-1} (Medetomidine 20 mg mL^{-1}), butorphanol 0.3 mg kg^{-1} (Butorphanol 50 mg mL^{-1}), midazolam 0.2 mg kg^{-1} (Midazolam 50 mg mL^{-1}), and hyaluronidase 1250 IU (Hyalase), all drugs sourced from Kyron Laboratories (Pty) Ltd, South Africa. Once the selected lion was feeding calmly at the carcass, it was darted from a vehicle intramuscularly (IM) in the upper hind leg or shoulder area using a CO_2 pressurised dart gun (Dan-Inject International) from a distance of 10–20 m. The times to initial effect, sternal and lateral recumbency following the administration of the immobilising drugs were recorded. A descriptive score ranging from 1 (excellent) to 4 (poor) was used to assess induction quality (Table 1). It was noted if the animal had to