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Encarna Casas-Díaz, Ignasi Marco, Jorge R. López-Olvera, Gregorio Mentaberre, Santiago Lavín. Comparison of xylazine-ketamine and medetomidine-ketamine anaesthesia in the Iberian ibex (). European Journal of Wildlife Research, 2011, 57 (4), pp.887-893. 10.1007/s10344-011-0500-7. hal-00667595

HAL Id: hal-00667595

<https://hal.science/hal-00667595>

Submitted on 8 Feb 2012

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Comparison of xylazine–ketamine and medetomidine–ketamine anaesthesia in the Iberian ibex (*Capra pyrenaica*)

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Received: 6 October 2010 / Revised: 13 January 2011 / Accepted: 17 January 2011 / Published online: 8 February 2011
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Abstract A comparison was made between two anaesthetic combinations in 35 free-ranging adult Iberian ibexes (*Capra pyrenaica*), from May to December 2005. Sixteen ibexes (10 males, 6 females) were captured using xylazine–ketamine ($3.0 \pm 0.4 + 3.0 \pm 0.4$ mg/kg) and 19 ibexes (12 males, 7 females) with medetomidine–ketamine ($0.10 \pm 0.02 + 2.1 \pm 0.3$ mg/kg). Anaesthetic times were evaluated, as well as clinical variables (respiratory and heart rates, rectal temperature, haemoglobin oxygen saturation), haematological and biochemical variables, at the time of induction and after 1 h. The heart rate of ibex immobilized with medetomidine–ketamine was higher than those immobilized with xylazine–ketamine. Stabilization of the heart rate of ibex immobilized with medetomidine–ketamine came earlier than those immobilized with xylazine–ketamine. Rectal temperature decreased and stabilized in both groups, but earlier in the xylazine–ketamine group, and hypoxemia was observed in both groups. The white blood cell count of ibex immobilized with medetomidine–ketamine was lower than those immobilized with xylazine–ketamine throughout anaesthesia, while sodium concentration was higher only after 1 h of anaesthesia. In ibex immobilized with xylazine–ketamine, the neutrophil count, serum creatinine kinase activity and aspartate aminotransferase activity increased after 1 h of immobilization, while triglycerides decreased. Changes found in haematological and biochemical variables suggest no

major differences in the different drug combinations used, but clinical findings of this study, as well as hypoxemia, hypothermia and bradycardia, were important records that should be taken into account when performing a safe operation.

Keywords Anaesthesia · *Capra pyrenaica* · Iberian ibex · Medetomidine · Ketamine · Xylazine

Introduction

Anaesthesia is useful for handling of species that are highly sensitive to stress or especially aggressive. However, it does not completely eliminate or prevent stress or capture myopathy, possibly due to pursuit of the animal before and after the anaesthetic drug injection (Harthoorn 1982; Jessup 1999).

For anaesthesia in the domestic goat, single-drug protocols or a combination of drugs from two anaesthetic groups have been used (Pawde et al. 1996; Afshar et al. 2005; Mahmood and Mohammad 2008). The use of a single anaesthetic drug is very rare in wildlife, it being more common to associate two or more drugs to obtain the desired effect. The most frequently used anaesthetic combinations in wild ungulates are ketamine–xylazine, etorphine–acepromazine, tiletamine–zolazepam and medetomidine–ketamine (Caulkett and Haigh 2007). Either xylazine or medetomidine, in combination with ketamine, are used in different ungulate species, such as aoudads (*Ammotragus lervia*), mouflon (*Ovis musimon*), axis deer (*Cervus axis*), fallow deer (*Cervus dama*), common red deer (*Cervus elaphus*), Pere David's deer (*Elaphurus davidianus*) and Alpine ibex (*Capra ibex ibex*) (Golightly

Communicated by F. Kaup

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and Hofstra 1989; Jalanka and Roeken 1990; Peinado et al. 1999).

The Iberian ibex (*Capra pyrenaica*) is used in translocations and ecological studies in Spain, for which its capture is common practice. The species has a marked sexual dimorphism with higher body weight and larger horns in males, making handling difficult and involving personal risk when using physical capture methods. Risks are lower if teleanaesthesia is used for animal immobilization. The application of different anaesthetic combinations and methods provides new, hitherto unpublished, information for this species, thus facilitating the choice of chemical anaesthesia and method involving the lowest risk for both humans and animals.

In this study, two anaesthetic combinations—xylazine–ketamine (XK) and medetomidine–ketamine (MK)—were studied to determine differences in anaesthetic times, as well as clinical, haematological and biochemical variables in the free-ranging Iberian ibex.

Materials and methods

Thirty-five adult Iberian ibexes were captured in the Sierra Nevada National Park, (El Toril estate, 37°03'N, 3°34'O), in Southern Spain, from May to November 2005. The animals were immobilized by remote darting using a CO₂ powered rifle (DAN-Inject, model JM Special, Børkop, Denmark) within a corral trap. The anaesthetic combinations used were xylazine (3.0±0.4 mg/kg, mean ± SD) (Xilagesic® 20%, 200 mg/ml, Laboratorios Calier, Barcelona, Spain) with ketamine (3.0±0.4 mg/kg, mean ± SD) (Imalgène® 1000, 100 mg/ml, Merial, Lyon, France) in 16 animals (10 males, 6 females), and medetomidine (0.10±0.02 mg/kg, mean ± SD) (Zalopine®, 10 mg/ml, Orion Pharma, Espoo, Finland) with ketamine (2.1±0.3 mg/kg, mean ± SD) in 19 animals (12 males, 7 females). Administered intramuscularly antagonist doses were 1 mg atipamezole (Antisedan®, Orion Pharma, Espoo, Finland) per 10 mg xylazine, and 5 mg atipamezole per 1 mg medetomidine. The mean body weight ±SD was 52.0±11.4 and 28.9±4.5 kg for males and females, respectively. Five days were necessary to capture the animals (3 days in May and 2 days in November 2005).

The Iberian ibexes were captured in a corral trap (100×50 m) baited with food to attract them the day before the intervention. Once inside, an anaesthetic dart with a standard dose according to estimated body weight was prepared and shot with the dart rifle from a covered feeder. After induction, the animal was placed in a transport sack net, with a 4×4 cm mesh (Ziboni Ornitecnica, Bergamo, Italy), transported outside the enclosure and weighed. The precordial region was shaved to install a heart rate monitor transmitter (Polar Vantage NV and S710i Polestar, Elect

Polestar Oy, Kempele, Finland). Ultrasonography gel was used to ensure good contact between the electrodes and the skin (Geleco®, Novartis, Barcelona, Spain). The receiver was placed in a plastic collar around the neck, since it must be less than 1.5 m from the transmitter. In addition, rectal probes to record temperature were used (Mätman data-logger®, Chipsobits Eltex AB, Osby, Sweden).

The heart rate monitor was left in place for 43.9±11.5 min (mean ± SD) and rectal probes for 40.0±11.2 min (mean ± SD). Both variables were recorded every 60 s, the recorded series being saved and turned into numerical values with their respective software. For statistical analysis, a mean value for every 5 min was calculated for both heart rate and rectal temperature. Stability times were calculated in the heart rate and temperature. These times were determined comparing the values along the period of study and establishing as time of stabilization the minute from which differences were not statistically significant with the following minutes.

Respiratory rate and haemoglobin oxygen saturation was monitored every 10 min throughout anaesthesia. The respiratory rate was determined by direct observation of the costal wall movements; haemoglobin oxygen saturation was measured with a pulse oximeter with a probe attached to tongue (Vet/Ox® 4404, Heska Corporation, Fort Collins, Colorado, USA). Time of initial effect was defined as the interval between the time of darting and onset of ataxia. Time to recumbency was the interval between darting and the time that the ibex lay down in sternal recumbency. The time from darting to safe handling of animals was defined as induction. After 1 h of induction, the antagonist was administered. First arousal was defined as the point when the animal began to lift its head. The time from atipamezole administration up to when the animal returned to a standing position and ambulation, with some minor ataxia, was defined as recovery.

Blood samples were collected from the jugular vein when the animal was anesthetized (T0) and after 1 h (T1). Two millilitres were placed in commercial tubes containing tripotassium ethylenediaminetetraacetic acid (EDTA) as anticoagulant. The remaining blood was placed in tubes with polystyrene granules to facilitate coagulation and serum separation. The samples were kept in a portable refrigerator for processing, always within 12 h.

Animal care activities and study procedures were conducted in accordance with the guidelines of the good experimental practices, under the approval of the Ethical and Animal Welfare Committee of the Universitat Autònoma of Barcelona.

Red blood cell count (RBC), white blood cell count (WBC), platelet count and haemoglobin concentration were determined with an electronic impedance semi-automatic analyzer (Sysmex F-800; Toa Medical Electronics, Hamburg, Germany). Packed cell volume (PCV) was measured by the

Table 1 Mean $\pm$ SD (min–max) of comparative immobilization anaesthetic times of xylazine–ketamine and medetomidine–ketamine combinations in Iberian ibexes

	Xylazine+ketamine	Medetomidine+ketamine
Initial effect (min)	2.6 $\pm$ 0.8 (1–4)	5.7 $\pm$ 4.7 (2–20)
Recumbency (min)	5.4 $\pm$ 3.2 (1–13)	8.7 $\pm$ 5.6 (3–24)
Induction (min)	8.2 $\pm$ 4.1 (2.5–15)	11.6 $\pm$ 7.4 (3.75–30)
Antagonist (min)	70.9 $\pm$ 4.0 (65–80)	71.3 $\pm$ 5.3 (65–81)
First arousal (min)	2.7 $\pm$ 0.6 (1.72–3)	5.9 $\pm$ 4.9 (1.72–20)
Recovery (min)	4.6 $\pm$ 5.2 (0–20)	5.2 $\pm$ 1.4 (2.5–7)

standard microhaematocrit method, using a microhaematocrit centrifuge (Haematospin 1400, Hawksley, Sussex, UK) at 14,000 G for 6 min. Mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH) and mean corpuscular haemoglobin concentration (MCHC) were calculated from the RBC, haemoglobin concentration and PCV. The differential leukocyte count was made by identifying 200 leukocytes with an optical microscope at an original magnification of $\times 1000$, in blood smears dried with a panoptic stain (Chemical Applied Clinic, Tarragona, Spain). The serum was obtained after centrifuging the clotted samples at 1,811 G, and was frozen at -20°C awaiting analysis. Biochemical variables such as enzymes [creatinine kinase (CK), aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline lactate dehydrogenase (LDH), alkaline phosphatase (AP)], metabolites (urea, glucose, cholesterol, triglycerides, total bilirubin, lactate, creatinine), as well as total proteins and chloride, were measured with two automatic analyzers (Cobas Mira[®], Roche, Rotkreuz, Switzerland; Olympus AU400[®], Olympus, Mainz, Germany). Sodium and potassium were measured by flame photometry (Corning 410 C[®], Medical Corning Medfield, USA) and cortisol levels with an ELISA commercial kit (EIA-1887, DRG Instruments GMBH, Marburg, Germany).

The software SAS[®] for System V8 Windows (SAS Inc. Institute, Cary, North Carolina, USA) were used to statistical studies, which includes all procedures applied. Tests of normality of the times obtained throughout anaesthesia were carried out. The non-normal variables were transformed logarithmically and normality was analyzed again. Values regarded as outliers were discarded, care being taken not to exceed the maximum allowed by statistical studies. An analysis of variance (ANOVA) was applied to data considered normal to detect statistically significant differences between the groups using the PROC GLM procedure. The nonparametric data were analyzed with the PROC NPAR1WAY ANOVA procedure. The factor considered in this model for each variable was the anaesthetic combination used; the remaining data (clinical, haematological and biochemical values) were analyzed with an ANOVA, which compared the averages of repeated measures using the PROC MIXED procedure. The main factor was the treatment used, with either of the two anaesthetic combinations, and the repeated factor was time.

Least square means (LS MEANS) was used due to the unbalanced distribution of animals between groups. In all cases, the accepted level of significance was $p < 0.05$.

Results

Anaesthesia and recovery times are reported in Table 1. Some of the ibexes presented apneas up to 30 s. The heart rate remained stable and the temperature decreased over time in both groups (Fig. 1). The heart rate stabilized earlier in the group anaesthetized with MK (40 min) than in the

Fig. 1 **a** Heart rate and **b** temperature (mean values) in Iberian ibex immobilized with xylazine–ketamine or medetomidine–ketamine. Vertical arrows indicate stability times; minutes in box indicate significant ($p < 0.05$) differences between anaesthetic combinations

Table 2 Minimum and maximum values for the heart rate and the rectal temperature

	Heart rate	Temperature
Xylazine+ketamine	39.6–104.8	33.0–40.9
Medetomidine+ketamine	40.4–114.0	35.1–42.8

XK group (45 min), and decreased and remained lower for the last 20 min of the study in animals immobilized with MK. The temperature stabilized earlier in the group anesthetized with XK (25 min) than in the MK group (40 min) (Fig. 1). Minimum and maximum values for the heart rate and the rectal temperature are shown in Table 2. Table 2 and changes in respiratory rate and haemoglobin oxygen saturation in Figure 2.

The MCV decreased significantly over time in the MK group, and the leukocyte counts was lower than in the XK group throughout the study. The neutrophil counts increased significantly over time in the group anesthetized with XK (Fig. 3).

Triglycerides decreased, and creatine kinase (CK) and aspartate aminotransferase (AST) increased over time in the XK group. Sodium concentration was higher in the group anesthetized with MK at the end of the study as compared with the XK group (Fig. 4).

Fig. 2 **a** Respiratory rate and **b** haemoglobin oxygen saturation in Iberian ibex immobilized with xylazine–ketamine or medetomidine–ketamine **Fig. 3** **a** Mean corpuscular volume (MCV), **b** white blood cells count (WBC) and **c** neutrophils during anaesthesia of Iberian ibex. *a*, *b* means with different superscript statistically different ($p < 0.05$) from each other. Asterisks indicate statistically significant differences ($p < 0.05$) between anaesthetic combinations

Discussion

Anaesthetic agents reported for use in Iberian ibex include etorphine (Pérez et al. 1999), tiletamine–zolazepam (Peinado et al. 1993, Santiago-Moreno et al. 2011), detomidine–ketamine (Santiago-Moreno et al. 2011) and the XK combination (Peinado et al. 1991). For similar species, such as Alpine ibex (*Capra ibex*), carfentanil and xylazine

(Kreeger and Arnemo 2002) and the Hellabrunner mix (125 mg xylazine+100 mg ketamin/ml) (Abderhalden et al. 1998) have also been used, but care must be taken in some species of wild ungulates that have a special sensitivity (Wiesner and von Hegel 1985).

Haematological and serum biochemical variables in studies with Iberian ibex were similar to those obtained in our study, but a few differences should be mentioned. In the study of XK-immobilized ibexes, only RBC and lymphocytes were higher, and HCM was lower. The greatest differences are found with ibexes immobilized with tiletamine–zolazepam (Peinado et al. 1993), which had a lower MCHC, neutrophil count, glucose concentration, urea, CK, AST and LDH, and a higher count of lymphocytes, monocytes and eosinophils. These differences may be due to pre-capture handling (box-traps previous to anaesthesia) and drugs administered. Santiago-Moreno et al. (2011) used a combination of another alpha-2-adrenergic agonist (detomidine) and ketamine, and obtained a lower induction and respiratory rate, a lower concentration of glucose, creatinine, AST and CK, and a

stable temperature. However, the ibexes used in this study were conditioned in a sand-floor stable for a period of 12 months, and hand injection was feasible.

The animals in our study displayed a higher respiratory rate (107 ± 36 breaths per minute) than in the Alpine ibex (*C. ibex*, 83 ± 15 breaths per minute) immobilized with xylazine (Peracino and Bassano 1993). Also, as in the previous report, the Iberian ibex in our study displayed several apneas lasting up to 30 s. Hypoxemia and compensatory tachypnea to balance the lack of oxygen could account for this difference. However, in ruminants, in addition to hypoventilation during anaesthesia, intrapulmonary causes (such as ventilation-perfusion mismatch, shunt and diffusion impairment) and recumbency can cause hypoxemia, which may effectively be treated with supplemental oxygen (Adamson and Mills 1996).

Both xylazine and medetomidine can cause hypotension and bradycardia, but medetomidine has ten times more specificity for alpha-2 receptors versus alpha-1 receptors when compared to xylazine (Gross and Booth 1995; Plumb

Fig. 4 **a** Serum creatine kinase (CK), **b** aspartate aminotransferase (AST), **c** triglycerides and **d** sodium during anaesthesia of Iberian ibex. *a*, *b* means with different superscript statistically different ($p <$

0.05) from each other. Asterisks indicate statistically significant differences ($p < 0.05$) between anaesthetic combinations

2008). In fact, Celly et al. (1997) found that xylazine did not affect the heart rate in sheep. In addition, Jalanka and Roeken (1990) found that medetomidine produces hypothermia in non-domestic mammals. There are no reference values for basal (resting) clinical parameters in the Iberian ibex. But, if we compare our results with the reference values given for domestic goats (Jackson and Cockcroft 2002), the heart rate and the body temperature of the Iberian ibex anesthetized with MK were lower, which could indicate bradycardia and hypothermia. Santiago-Moreno et al. (2011) found also bradycardia in ibexes treated with detomidine.

Changes found in haematological and biochemical variables in the Iberian ibex of our study suggest no major differences between the two drug combinations used. The decrease in the MCV in the group of MK and the increase in neutrophils and higher WBC in the group of XK is unlikely due to stress within treated groups because other changes in haematological variables such as RBC, PCV, concentration of haemoglobin and lymphocytes should have been expected. The increase in CK and AST in the XK group could be due to muscle necrosis caused by muscular injection or muscular contractions (Gaertner et al. 1987, Bouts et al. 2010). Also, the decrease of triglycerides and the lower concentration of sodium in the XK-immobilized ibex are difficult to relate with a different response to capture stress. These variables may not be useful as stress indicators, since some authors have found changes whereas others have not (Kocan et al. 1981; Broom and Johnson 1993; Peinado et al. 1993; Montané et al. 2003). Probably, other factors not considered in our study, such as season, nutrition and environmental temperature, may affect some of these variables, and it would be needed to be further analyzed. Hypoxemia, hypothermia and bradycardia were important findings recorded in this study. Safe anaesthesia includes prevention or treatment of physiological side effects. For this reason, if MK is used, oxygen supplementation is recommended. Further studies on arterial blood gases should be performed to improve the safety of these procedures.

Acknowledgements The authors would like to express their gratitude to the directors and rangers of the Sierra Nevada National Park for their invaluable collaboration. Thanks are also due to University students and volunteers for helping in the handling of the animals. This study was funded by Spanish government grant REN2001-1989/GLO.

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