



Evaluation of medetomidine, ketamine and buprenorphine for neutering feral cats

Kelly A Harrison ^{MS}¹, Sheilah A Robertson ^{BVMS (Hons), PhD, Diplomate ACVA, Diplomate ECVAA}^{1*}, Julie K Levy ^{DVM, PhD, DACVIM}², Natalie M Isaza ^{DVM}³

¹Department of Large Animal Clinical Sciences, College of Veterinary Medicine, University of Florida, PO Box 100136, Gainesville, FL 32610-0136, USA

²Maddie's Shelter Medicine Program, College of Veterinary Medicine, University of Florida, USA

³Merial Shelter Medicine Clerkship, Department of Small Animal Clinical Sciences, College of Veterinary Medicine, University of Florida, USA

A combination of medetomidine (M, 100 µg/kg), ketamine (K, 10 mg/kg) and buprenorphine (B, 10 µg/kg), administered by intramuscular injection, was evaluated for spaying and castration (neutering) of feral cats ($n = 101$). Eleven animals (11%) required supplemental anesthesia (isoflurane by mask) to maintain an adequate plane of surgical anesthesia. Atipamezole (A, 125 µg/kg) was administered subcutaneously at the completion of surgery. All cats recovered from surgery and were released the following day. A hemoglobin saturation (SpO₂) value of <95% was recorded at least once during anesthesia in all cats. This MKB combination can be used in a feral cat sterilization clinic, but isoflurane supplementation may be necessary. Further research is indicated to determine the clinical significance of the low SpO₂ values associated with this anesthetic regimen.

Date accepted: 10 June 2011

© 2011 ISFM and AAFP. Published by Elsevier Ltd. All rights reserved.

In the United States the presence of approximately 60–100 million feral cats is associated with a variety of problems including public health concerns and nuisance issues, as well as a significant loss of native wildlife.^{1,2} The welfare of the cats themselves is also an important issue.¹ One approach to reduce feral cat populations is trap–neuter–return (TNR).^{3–8} Trap–neuter–return programs present several challenges and rely heavily on the predictability and safety of anesthetic protocols. Cats are often of an unknown weight, age and health status and injectable protocols must be suitable for both males and females, render the cats unconscious while still inside their traps, provide adequate duration of action, analgesia and a rapid return to normal function.

The combination of tiletamine, zolazepam, ketamine, and xylazine (TKX) has been used for feral cat anesthesia because it is economical and easily administered.^{9,10} It is, however, associated with low hemoglobin oxygen saturation (SpO₂) values, prolonged recovery times, hypothermia, and inadequate postoperative analgesia.⁹ We hypothesized that a combination of medetomidine, ketamine, and buprenorphine (MKB) would offer several advantages over TKX for feral cat anesthesia.

Medetomidine (M) is a specific α_2 -adrenoceptor agonist and provides sedation, muscle relaxation, and analgesia.^{11,12} A major advantage of medetomidine is that its effects can be reversed with atipamezole. Ketamine hydrochloride (K), a short-acting dissociative anesthetic, has some analgesic activity and few cardiopulmonary depressant effects.¹³ Buprenorphine (B), a long-acting partial opioid analgesic, is considered highly suitable for perioperative pain management in cats.^{14–20}

The objective of this study was to evaluate the anesthetic and physiological effects of MKB in feral cats undergoing castration and ovariohysterectomy. The drug doses used were based on a review of the literature and a pilot study (unpublished data, Meyer K; Master's thesis; College of Veterinary Medicine, University of Florida 2007).

Materials and methods

Animals

This study was pre-approved by the University of Florida Institutional Animal Care and Use Committee. Feral cats ($n = 101$) admitted to two large-scale TNR programs in Florida (Operation Catnip and Maddie's Outdoor Cat Program) were used in this study. Cats

*Corresponding author. Tel: +1-352-294-4280; Fax: +1-352-392-8289. E-mail: robertsons@ufl.edu

were captured from local colonies using commercially available humane traps (Cat Trap number 106, Tomahawk Live traps) and underwent surgery at the University of Florida's College of Veterinary Medicine. Only apparently healthy cats, free from obvious signs of upper respiratory infection or diarrhea, were included. Based on size and appearance, most were assessed to be adults (≥ 1 year of age) ($n = 99$), but two cats estimated to be under 6 months of age ($n = 2$) were included.

Anesthesia

Each cat's weight was determined by subtracting the known trap weight from the combined weight of the trap plus cat. Each cat received a combination of medetomidine HCl; 100 $\mu\text{g}/\text{kg}$ (Domitor; Orion Corporation), ketamine HCl; 10 mg/kg (Ketaject; Phoenix Pharmaceuticals), and buprenorphine HCl; 10 $\mu\text{g}/\text{kg}$ (Buprenex; Reckitt Benckiser Healthcare) mixed in a single 1 ml or 3 ml syringe. In a 3 kg cat the total volume of injectate was 0.7 ml. The target injection site was the paralumbar muscles. If the first injection of MKB did not cause recumbency and lack of arousal when the trap was gently turned over, after 10 min, an additional dose of medetomidine (20 $\mu\text{g}/\text{kg}$) was injected intramuscularly. If anesthesia remained inadequate at 15 min an additional dose of ketamine (2.5 mg/kg) was injected intramuscularly. At the completion of surgery, each cat received 125 $\mu\text{g}/\text{kg}$ of atipamezole HCl (Antisedan; Orion Corporation, Espoo) subcutaneously between the scapulae. Atipamezole was repeated if a cat had not achieved sternal recumbency within 1 h.

Data collection

When cats showed no response to squeezing of their digits they were removed from their traps. A pulse oximeter sensor (Nellcor Puritan Bennett NPB-40, Nellcor Puritan Bennett) was placed on the tongue to monitor SpO_2 and pulse rate. Heart rate was also recorded by direct auscultation. Indirect blood pressure was measured using a Doppler flow detector (Ultrasonic Doppler Flow Detector, Model 811-B and 811-L, Parks Medical Electronics). The hair over the palmar aspect of the carpus was shaved and conductive ultrasound gel was applied to the Doppler probe which was secured directly over the digital arteries. An appropriately sized (cuff width approximately 40% of the circumference of the forelimb) blood pressure cuff (Classic-CUF; Critikon) was applied proximally and attached to a sphygmomanometer (DuraShock Handheld aneroid sphygmomanometer, Welch Allyn). The pressure (mmHg) at which the first audible sound returned during cuff deflation was recorded as the systolic blood pressure; a reading of <90 mmHg was considered hypotensive. Respiratory rate was counted by observation and rectal

temperature was acquired using a standard electronic thermometer (MABIS Healthcare).

A sterile petroleum-based ophthalmic lubricant (Akwa Tears; Akorn) was applied to both eyes. Approximately 0.5 cm of the distal tip of the left ear was removed for identification purposes using a sterile hemostat and surgical scissors. The hair was clipped (females) or plucked (males) from the surgery site and the skin was prepared for surgery using alternating povidone iodine scrub solution and alcohol. Surgeries were aseptically performed and cats were also vaccinated and given medications for internal and external parasites as previously described.¹⁰ Systolic blood pressure (BP), respiratory rate (RR), SpO_2 and pulse rate (PR) was recorded at 5-min intervals following MKB injection. Temperature was measured at the time of induction, at the completion of surgery, and 5 min following atipamezole injection.

Cats were administered supplemental anesthesia (isoflurane in oxygen delivered by mask using a non-rebreathing system) if a response occurred which was related to application of a noxious stimulus; for example, limb withdrawal in response to squeezing of the digits of the pelvic limbs prior to the start of surgery, movement in response to a towel clamp or during surgery. The need for additional injectable anesthesia or the need for supplemental inhalational anesthesia was recorded for each cat.

Time intervals recorded were; MKB injection to lateral recumbency, MKB injection until start of surgery, surgical duration, atipamezole injection to sternal recumbency, and total time recumbent. Apneustic breathing and periods of apnea (defined as temporary cessation of breathing for more than 1 min) were also recorded.

Statistical analysis

SAS PROC MIXED (SAS Institute) was used to analyze data. Time intervals were compared separately over time by means of a two-factor ANOVA (time-fixed; subject-random) test. Temperatures were compared over time using split-plot repeated measures ANOVA with post hoc time comparisons by means of Bonferroni's *t*-test.

Comparisons between groups for time to surgery and duration of surgery were by means of Wilcoxon rank sum test.

The effect of more than one dose of MKB on total time recumbent was evaluated using a two-way ANOVA test. Reversal to sternal time was compared between cats that did or did not require additional MKB by means of an unpaired *t*-test.

The difference between physiological variables upon the completion of surgery and 5 min following atipamezole administration were compared in all cats. Changes in physiological variables (BP, RR, PR, and SpO_2) before and after the reversal of medetomidine were analyzed using split-plot repeated measures ANOVA. The significance level was set at

$P < 0.05$. Data are shown as the mean \pm standard deviation (SD).

Results

Animals

A total of 53 males and 48 females were anesthetized with MKB. Two cats were pregnant, two cats were lactating, and three cats were already sterilized (one male, two females). These cats were included in data analysis. There was no significant difference in the weight of male cats (3.2 ± 0.2 kg) compared with female cats (2.9 ± 0.1 kg).

Need for additional anesthesia

Eleven cats required a second injection of medetomidine plus or minus ketamine. Seven male cats received an additional injection of medetomidine, and of these seven, three also received additional ketamine. Four females received additional medetomidine and of those four, two also received ketamine. Eleven cats (two males, nine females) required supplemental inhalational anesthesia. Females required supplemental anesthesia significantly more often than males. Five of the nine females required inhaled supplementation at some point after 45 min of successful injectable anesthesia.

Adverse events

All cats were discharged alive from the clinic. Eight cats (two males, six females) vomited within 5 min of MKB injection. In six males a rapid, shallow breathing pattern began immediately after induction and remained throughout surgery. Obvious apneustic breathing was observed in three males. Eight males responded momentarily to the stimulus of castration surgery (tension on the spermatic cord) by displaying hind limb movements. Spontaneous movement (paw extension and ear flicking) unrelated to a noxious stimulus was observed in three females. Post-induction apnea was observed in one cat. Retching ($n = 1$) and pawing at the mouth ($n = 6$) in the post-reversal period were also observed. One male cat had a SpO_2 value below 70% 10 min after injection and appeared cyanotic. Administration of oxygen by mask increased SpO_2 values but the highest value recorded was 83%.

Time intervals

MKB induced lateral recumbency in 4.3 ± 4 and 5.2 ± 5.6 min in male and female cats, respectively. There was no significant difference in time to lateral recumbency between males and females. The time (in minutes) from MKB injection until the start of surgery was significantly longer in females (median 23, 25th and 75th interquartile range 19.6 and 25.4,

respectively) compared to males (median 15, 25th and 75th interquartile range 13 and 19, respectively). Similarly, surgical duration (in minutes) was significantly longer in female (median 22.3, 25th and 75th interquartile range 18 and 39.8, respectively) compared to male cats (median 2.4, 25th and 75th interquartile range 1.0 and 4.5, respectively).

Fourteen (six males, eight females) cats were given a second injection of atipamezole. Time from injection of atipamezole until time to sternal recumbency was 33.4 ± 31.1 min for all cats and was not significantly different between males and female cats. There was no difference in time to sternal recumbency in cats that received a second dose of medetomidine plus or minus ketamine ($n = 11$) compared to those that received only one injection of MKB. There was also no association between cats that received additional medetomidine plus or minus ketamine and cats that required a second injection of atipamezole.

The total time recumbent (including preparation, surgery, and recovery) was significantly longer in females (86.9 ± 27.1 min) compared to males (64.7 ± 36.2 min).

Physiological variables – blood pressure, pulse rate, respiratory rate, SpO_2 , during anesthesia (Table 1)

Blood pressure in males (range 91–195 mmHg) did not change significantly over time. Blood pressure in females (range 38–190 mmHg) decreased significantly over time. Three female cats were considered to be hypotensive. One had a systolic blood pressure between 50 and 70 mmHg from 25 to 80 min, one had a reading of 60 mmHg at 50 min and the third cat had readings of 38, 60 and 66 mmHg at 35, 40 and 45 min post-injection. Twenty-two cats (seven females, 15 males) had a blood pressure measurement of >160 mm Hg at least once during anesthesia.

Pulse rate in males (range 77–176 beats/min) did not significantly change over time. Pulse rate in females (range 57–172 beats/min) significantly decreased over time. One female cat had severe bradycardia (pulse rate <60 beats/min) throughout anesthesia.

Hemoglobin oxygen desaturation was observed in both males (range 36–99% SpO_2) and females (range 73–100% SpO_2) at the first recording time (5 min after administration of MKB). SpO_2 increased significantly over time in both males and females. There was no significant change in respiratory rate during anesthesia in males (range 4–76 breaths/min) or females (range 4–56 breaths/min).

Physiological variables (blood pressure, pulse rate, respiratory rate, SpO_2) before and after reversal (Table 2)

Physiological variables obtained following the completion of surgery (pre-reversal) and 5 min following the administration of atipamezole (post-reversal) were

Table 1. Mean \pm SD blood pressure, pulse rate, SpO₂, and respiratory rate in male ($n = 53$) and female ($n = 48$) cats following injection of medetomidine, ketamine and buprenorphine.

Variable (units of measurement)	Sex	Time (min)																
		5	10	15	20	25	30	35	40	45	50	55	60	65	70	75	80	
Blood pressure (mmHg)	Male	152 \pm 21	157 \pm 22	152 \pm 19	145 \pm 24	135 \pm 34	138 \pm 26											
	Female	150 \pm 20	150 \pm 21	142 \pm 24	137 \pm 23	139 \pm 23	131 \pm 25											
Pulse rate (bpm)	Male	129 \pm 20	130 \pm 20	129 \pm 20	117 \pm 23	126 \pm 15	116.5 \pm 13											
	Female	134 \pm 15	125 \pm 20	133 \pm 15	128 \pm 17	121 \pm 19	118 \pm 19											
SpO ₂ (%)	Male	81 \pm 15	87 \pm 11	90 \pm 5	91 \pm 4	92 \pm 3	90 \pm 4											
	Female	87 \pm 6	91 \pm 4	90 \pm 4	91 \pm 5	92 \pm 5	92 \pm 4											
Respiratory rate (breaths/min)	Male	23 \pm 15	23 \pm 14	22 \pm 11	26 \pm 14	26 \pm 16	32 \pm 23											
	Female	18 \pm 10	20 \pm 7	20 \pm 9	21 \pm 8	20 \pm 7	19 \pm 8											

compared. Time of reversal was at 25 ± 7 (range 14–41) and 55 ± 20 (range 29–113) min after administration of MKB in males and females, respectively. Male and female blood pressures changed significantly over this time period. Blood pressures in females were less than blood pressures in males in both the pre-reversal and post-reversal periods. Blood pressure was significantly lower post-reversal when compared to pre-reversal values in both males and females.

Pre-reversal pulse rate values in males were significantly greater than in females. There was no difference between male and female pulse rates in the post-reversal period. Pulse rate values significantly increased after reversal in both males and females.

SpO₂ values increased in males and females following administration of atipamezole. SpO₂ values were significantly lower in male cats at the time of reversal and post-reversal when compared to female cats.

Rectal temperature

Rectal temperature was lower in females following induction, at the time of reversal, and post-reversal compared to males. Temperature overall decreased as a function of time in both males and females. Induction, pre-reversal, and post-reversal temperatures in males were $38.9 \pm 0.6^\circ\text{C}$, $38.2 \pm 0.7^\circ\text{C}$, $37.9 \pm 0.7^\circ\text{C}$ and $38.7 \pm 0.5^\circ\text{C}$, $36.8 \pm 1.1^\circ\text{C}$, $36.7 \pm 1.2^\circ\text{C}$ in females, respectively. No rectal temperature below 34°C was recorded in male cats. One female had a temperature of 33.1°C postoperatively. Compared to values in the pre-reversal period, temperatures in the post-reversal period were significantly lower in males, but not in females.

Discussion

The protocol used in this study was considered relatively easy to administer, although the total volume of injectate was greater than in studies using TKX.⁹ Approximately 11% of cats required supplemental anesthesia with isoflurane. This may be due to either incomplete intramuscular delivery or unmet anesthetic requirements and individual variations in response to anesthetic drugs. Female cats had a greater need for 'rescue' anesthesia probably due to lengthier preparation and surgical procedure times.

Decreased respiratory rate and apnea have been described previously in up to 80% of cats that received medetomidine and ketamine.^{21,22} A decrease in SpO₂ in the first 5 min following MKB administration was common in the present study. One male cat had a SpO₂ value of 36% following MKB administration, but responded to oxygen delivered via a face mask; despite the low SpO₂ values in many cats, only this cat appeared cyanotic when the oral mucus membranes were visualized. Medetomidine often results in pale mucous membrane color due to vasoconstriction and this was observed in our study. Making

Table 2. Mean \pm SD blood pressure (BP), pulse rate (PR), SpO₂, and respiratory rate (RR) in male ($n = 53$) and female ($n = 48$) cats before and after injection with atipamezole (reversal). Time of reversal was 27 ± 7 min after administration of MKB in males and 55 ± 20 min in females. Time between recordings was 5 min.

Variable (units of measurement)	Sex	Before reversal	After reversal
BP (mmHg)	Male	148 \pm 21	108* \pm 18
	Female	123 [†] \pm 24	89* [†] \pm 20
PR (bpm)	Male	124 \pm 23	135* \pm 23
	Female	106 [†] \pm 18	128* \pm 20
SpO ₂ (%)	Male	91 \pm 4	93* \pm 3
	Female	94 [†] \pm 3	96* [†] \pm 2
RR (breaths/min)	Male	31 \pm 16	31 \pm 15
	Female	24 \pm 9	26 \pm 9

*Denotes a significant difference before and after reversal.

[†]Denotes a significant difference between males and females.

assumptions of the cat's oxygenation status based on mucus membrane color may be misleading. In addition, pulse oximetry is not always a reliable method for predicting oxygen saturation of arterial blood in patients when vasoactive drugs are administered.²³ Severe vasoconstriction, low cardiac output, and hypotension reduce the pulsatile volume of blood in peripheral tissues which reduces signal strength and quality of the pulse; this can lead to inaccurate values as the sensor has difficulty distinguishing background noise from true signal. Alpha₂-agonist drugs increase pulmonary vascular resistance and decrease cardiac output, thus, another explanation for the low SpO₂ values observed in this study may have been the result of ventilation perfusion mismatch together with hypoventilation while breathing room air. We did not collect arterial blood samples in this study, therefore, we do not know what the PaO₂ values were in these cats. A low SpO₂ or hypoxemia could result in abnormal organ function or cellular damage²⁴; however, in this study it was not possible to determine if there were adverse consequences.

In a previous study of MKB in cats which used a lower dose of medetomidine (40 μ g/kg), SpO₂ values were $94 \pm 4\%$.²⁵ These values also increased over time, probably due to the waning effects of the medetomidine. While low SpO₂ values may increase in response to supplemental oxygen, either by face mask or after intubation, this is generally not feasible in large-scale TNR clinics due to equipment limitations and large numbers of cats undergoing anesthesia at the same time. In addition, monitoring equipment is rarely available for all cats at all times in large scale TNR clinics, therefore, identifying cats with a low SpO₂ is a challenge. The consequences of low SpO₂ levels in cats anesthetized with MKB are unknown.

In one study, heart rate in cats administered only medetomidine (80–110 μ g/kg) decreased to about 50% of baseline values within 15–30 min.²⁶ When medetomidine (80 μ g/kg) and ketamine (5 mg/kg) were

combined and given by intramuscular injection, heart rate was decreased by 31% and blood pressure increased by 69% at 5 min compared to awake values.²⁷ Although we were unable to measure heart rate or blood pressure in conscious feral cats, the values and trends in these variables during the first 30 min after drug administration were similar to those reported by Dobromylskyj.²⁷

In our study, there were no changes in heart rate in response to surgical stimulation. In one study using medetomidine (80 μ g/kg) with ketamine (10 mg/kg) the authors reported no reflex responses to traction of the ovarian pedicles.²¹ In another study where medetomidine (80 μ g/kg) was combined with ketamine at 5, 7.5 or 10 mg/kg there did not appear to be an increase in heart rate related to ovariectomy and the authors stated these combinations provided 'satisfactory analgesia in deep organs' based on the lack of a 'pain reflex in response to traction of the ovarian pedicles' although they do not state what is meant by a 'pain reflex'.²² The absence of changes in heart rate in response to surgery could indicate that the depth of anesthesia was adequate in these cats; however, because medetomidine is a sympatholytic agent it could prevent sympathetic responses to noxious stimuli. In our feral cat clinic we observe carefully for movement in response to a noxious stimulus and if this occurs we provide additional anesthesia using isoflurane by mask.

When blood pressure is measured during anesthesia in cats this is usually done using non-invasive techniques. By convention, when using the Doppler ultrasonic method, the pressure that correlates to the first audible sound during cuff deflation is the systolic blood pressure. Grandy et al²⁸ reported that the systolic blood pressure measured by the Doppler ultrasonic technique was significantly lower, by 14 mmHg than that recorded from a catheter placed in the femoral artery. In another study, the Doppler technique underestimated systolic blood pressure and was relatively inaccurate for obtaining this

measurement; however, it was a good predictor of direct mean arterial pressure.²⁹ Therefore, although we considered three female cats to be hypotensive (systolic blood pressure <90 mmHg) at some time point during anesthesia their direct blood pressure may have been higher than recorded by our technique.

Cats administered MKB became hypothermic, similar to results reported with the use of tiletamine, zolazepam, xylazine and ketamine (TKX) in feral cats.^{9,10} Even mild hypothermia can substantially prolong recovery times by decreasing hepatic and renal blood flow, slowing drug metabolism and elimination.³⁰ Medetomidine elimination appears to rely heavily on biotransformation and is likely influenced by hepatic blood flow and temperature.³¹ The application of external heat sources during surgery and recovery may decrease recovery times; however, a logistical barrier arises when high numbers of cats are undergoing surgery and recovery simultaneously. In addition, the ability to apply external heat sources from outside the trap is limited.

Immediate postoperative analgesia was assumed to be adequate in most cats, but assessment of pain was not a primary goal of this study. Several studies have noted the efficacy of buprenorphine for up to 6 h following administration.^{19,20} There are no validated methods for pain assessment in cats, which makes evaluation and treatment difficult,³² particularly in feral cats. Restrictions for assessing pain in feral cats include the inability to palpate the surgical site and evaluate a response, and clearly differentiating fear and stress behaviors from pain behaviors.

Recovery times after MKB were shorter compared to TKX. Time to sternal recumbency was 72 ± 42 min in cats administered TKX⁹ and 33.4 ± 31.1 min in the current study. Atipamezole administration appeared to effectively reverse the effects of medetomidine, as evident by the significant increase in heart rate and decrease in blood pressure in the post-reversal period; similar changes have been reported within 5 min of reversal.²⁷ An unusually fast recovery may occur when larger doses of atipamezole are administered. In our experience, very rapid recoveries may result in physical trauma as a result of hyperexcitability; therefore, we administered atipamezole subcutaneously and at a lower dose than that suggested by the manufacturer. Relapse to sedation is not believed to be the cause for the need of additional atipamezole injections in some cats, as the half-life of atipamezole is twice that of medetomidine.³³ Interestingly, there was no relationship between cats that received supplemental doses of MKB and cats that required an additional injection of the reversal agent.

The combination of MKB provided adequate duration of action in most cats and the number of cats requiring isoflurane supplementation (11%) was considered acceptable for the operation of the large volume TNR clinic of this study and most commonly occurred more than 45 min after injection with MKB.

Knowing that 11% of cats may need supplemental anesthesia if their surgery is delayed or prolonged, allows planning of the timing and numbers of cats being anesthetized at any one time based on the availability of surgeons and anesthesia machines.

The MKB combination in this study appears to offer several advantages. The use of atipamezole allows for rapid reversal of the depressant effects produced by medetomidine. The injectable protocol was predictable, offered an acceptable duration of action, and a relatively rapid return to normal function. A relatively large injection volume is a potential disadvantage for the intramuscular route of administration in feral cats, but was not a problem in this study. MKB fulfilled many requirements associated with feral cat sterilization clinics; however, it displayed side effects of unknown consequence.

Acknowledgments

The authors would like to thank Dr Joe Hauptman, Michigan State University for statistical analysis and Mark Szarowicz for technical assistance.

References

- Jessup DA. The welfare of feral cats and wildlife. *J Am Vet Med Assoc* 2004; **225**: 1377–83.
- Case JB, Chomel B, Nicholson W, Foley JE. Serological survey of vector-borne zoonotic pathogens in pet cats and cats from animal shelters and feral colonies. *J Feline Med Surg* 2006; **8**: 111–7.
- Mahlow JC, Slater MR. Current issues in the control of stray and feral cats. *J Am Vet Med Assoc* 1996; **209**: 2016–20.
- Levy JK, Crawford PC. Humane strategies for controlling feral cat populations. *J Am Vet Med Assoc* 2004; **225**: 1354–60.
- Foley P, Foley JE, Levy JK, Paik T. Analysis of the impact of trap–neuter–return programs on populations of feral cats. *J Am Vet Med Assoc* 2005; **227**: 1775–81.
- Patronek GJ. Free-roaming and feral cats – their impact on wildlife and human beings. *J Am Vet Med Assoc* 1998; **212**: 218–26.
- Levy JK, Gale DW, Gale LA. Evaluation of the effect of a long-term trap–neuter–return and adoption program on a free-roaming cat population. *J Am Vet Med Assoc* 2003; **222**: 42–6.
- Zaunbrecher KI, Smith RE. Neutering of feral cats as an alternative to eradication programs. *J Am Vet Med Assoc* 1993; **203**: 449–52.
- Cistola AM, Golder FJ, Centonze LA, McKay LW, Levy JK. Anesthetic and physiologic effects of tiletamine, zolazepam, ketamine, and xylazine combination (TKX) in feral cats undergoing surgical sterilization. *J Feline Med Surg* 2004; **6**: 297–303.
- Williams LS, Levy JK, Robertson SA, Cistola AM, Centonze LA. Use of the anesthetic combination of tiletamine, zolazepam, ketamine, and xylazine for neutering feral cats. *J Am Vet Med Assoc* 2002; **220**: 1491–5.
- Savola JM, Ruskoaho H, Puurunen J, Salonen JS, Karki NT. Evidence for medetomidine as a selective and potent

- agonist at α_2 -adrenoreceptors. *J Auton Pharmacol* 1986; **6**: 275–84.
12. Virtanen R, Savola JM, Saano V, Nyman L. Characterization of the selectivity, specificity and potency of medetomidine as an α_2 -adrenoceptor agonist. *Eur J Pharmacol* 1988; **150**: 9–14.
 13. Lin HC. Dissociative anesthetics. In: Tranquilli WJ, Thurmon JC, Grimm KA, eds. *Lumb and Jones' veterinary anesthesia*. 4th edn. Oxford: Blackwell Publishing, 2007: 301–53.
 14. Watson AD, Nicholson A, Church DB, Pearson MR. Use of anti-inflammatory and analgesic drugs in dogs and cats. *Aust Vet J* 1996; **74**: 203–10.
 15. Robertson SA, Taylor PM. Pain management in cats; past, present and future. Part 2. Treatment of pain: clinical pharmacology. *J Feline Med Surg* 2004; **6**: 321–33.
 16. Joubert KE. The use of analgesic drugs by South African veterinarians. *J S Afr Vet Assoc* 2001; **72**: 57–60.
 17. Dobbins S, Brown NO, Shofer FS. Comparison of the effects of buprenorphine, oxymorphone hydrochloride, and ketoprofen for postoperative analgesia after onychectomy or onychectomy and sterilization in cats. *J Am Anim Hosp Assoc* 2002; **38**: 507–14.
 18. Capner CA, Lascelles BD, Waterman-Pearson AE. Current British veterinary attitudes to perioperative analgesia for dogs. *Vet Rec* 1999; **145**: 95–9.
 19. Pascoe PJ. Opioid analgesics. *Vet Clin North Am Small Anim Pract* 2000; **30**: 757–72.
 20. Robertson SA, Lascelles BD, Taylor PM, Sear JW. PK-PD modeling of buprenorphine in cats: intravenous and oral transmucosal administration. *J Vet Pharmacol Ther* 2005; **28**: 453–60.
 21. Verstegen J, Fargetton X, Ectors F. Medetomidine/ketamine anaesthesia in cats. *Acta Vet Scand Suppl* 1989; **85**: 117–23.
 22. Verstegen J, Fargetton X, Donnay I, Ectors F. An evaluation of medetomidine/ketamine and other drug combinations for anaesthesia in cats. *Vet Rec* 1991; **128**: 32–5.
 23. Ibanez J, Velasco J, Raurich JM. The accuracy of the Biox 3700 pulse oximeter in patients receiving vasoactive therapy. *Intensive Care Med* 1991; **17**: 484–6.
 24. Haskins SC. Monitoring anesthetized patients. In: Tranquilli WJ, Thurmon JC, Grimm KA, eds. *Lumb and Jones' veterinary anesthesia*. 4th edn. Oxford: Blackwell Publishing, 2007: 533–58.
 25. Cistola AM, Golder FJ, Levy JK, Waas AM, Robertson SA. Comparison of two injectable anesthetic regimes in feral cats at a large volume spay clinic. Proceedings of the 27th Annual meeting of the American College of Veterinary Anesthesiologists; 2002 Oct 9–11; Orlando, Florida, USA: 43.
 26. Vaha-Vahe T. The clinical efficacy of medetomidine. *Acta Vet Scand Suppl* 1989; **85**: 151–3.
 27. Dobromylskyj P. Cardiovascular changes associated with anaesthesia induced by medetomidine combined with ketamine in cats. *J Small Anim Pract* 1996; **37**: 169–72.
 28. Grandy JL, Dunlop CI, Hodgson DS, Curtis CR, Chapman PL. Evaluation of the Doppler ultrasonic method of measuring systolic arterial blood pressure in cats. *Am J Vet Res* 1992; **53**: 1166–9.
 29. Caulkett NA, Cantwell SL, Houston DM. A comparison of indirect blood pressure monitoring techniques in the anesthetized cat. *Vet Surg* 1998; **27**: 370–7.
 30. Posner L. Perioperative hypothermia in veterinary patients. *Clinician's Brief* 2007: 19–23.
 31. Salonen JS. Pharmacokinetics of medetomidine. *Acta Vet Scand Suppl* 1989; **85**: 49–54.
 32. Cambridge AJ, Tobias KM, Newberry RC, Sarkar DK. Subjective and objective measurements of postoperative pain in cats. *J Am Vet Med Assoc* 2000; **217**: 685–90.
 33. Paddleford RR, Harvey RC. Alpha 2 agonists and antagonists. *Vet Clin North Am Small Anim Pract* 1999; **29**: 737–45.

Available online at www.sciencedirect.com

