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Research Article

Effect of Furosemide on Dexmedetomidine-Ketamine Anaesthesia in Cats

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Summary: The effects of intramuscular (IM) administrations of 10mcg/kg dexmedetomidine, followed 10 minutes later by either IM injection of 10mg/kg ketamine alone (DK) or with 2.5 mg/kg furosemide (DKF) were assessed in five healthy cats (3 males and 2 females) using selected anaesthetic indices (Time to onset of anaesthesia (OA), Duration of Analgesia (DA), Duration of Recumbency (DR), and Time to Standing (TS), as well as, changes in heart rate (HR), respiratory rate (RR) and rectal temperature (RT) , following loss of righting reflex, and at 10 min intervals for 60-minute. The OA for DKF group (2.2 ±0.45 min) was not significantly (P>0.05) different from that for DK group (2.4± 1.14 min). The DA (42.6 ±13.01min) and DR (71.6 ±17.94min) for DKF group were longer than respective values of DA (31.8± 14.3) and DR (51.2 ± 16.2min) for the DK group. The TS for DKF (3.6 ± 2.8 min) was shorter than TS (8.0±3.8) for DK. However, these differences were not statistically significant (P > 0.05). HR, RR and RT were from 84.8 ± 8.7 to 113.2±30.7 beats/min, 17.4± 6.2 to 48.8 ±12.1 breaths/min and from 36.0±0.5 to 37.6 ± 0.6°C (DKF); 96.0±19.4 beats/min, 24.8±19.1 to 71.2 ± 34.3 breaths/min and from 36.0±0.5 to 37.6 ± 0.6°C (DKF); 96.0±19.4 to 112.8± 44.3 beats/min, 24.8±19.1 to 71.2 ± 34.3breaths/min and from 35.1±1.2 to 37.6 ±0.8 °C (DK). There were no significant differences (P > 0.05) in the vital parameters between the DKF and DK treatments. The values for HR and RR for DKF were generally lower than those for DK group. It was concluded that concurrent administration of furosemide with dexmedetomidine- anaesthesia in cats prolonged the duration of analgesia and recumbency but had no effect on onset of anaesthesia. A cat on this anaesthetic combination concurrently placed on furosemide medication will therefore need to be carefully monitored until full recovery.

Keywords*: Anaesthesia, Cat, Combination, Dexmedetomidine, Ketamine, Furosemide*

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INTRODUCTION

Ketamine hydrochloride is a phencyclidine derivative which is commonly used in both human and veterinary medicine (Mercer *et al* ., 2009; Kurdi *et al* ., 2014; Berry, 2015). Unlike other currently used anaesthetic agents, ketamine stimulates the cardiovascular system thereby producing increased heart, arterial blood pressure and cardiac output (Kistner, 2018). Ketamine also has minimal effects on central respiratory drive and produces airway relaxation by acting on various receptors, inflammatory cascades and bronchial smooth muscles (Berry, 2015). Ketamine is licensed for use as a sole anaesthetic agent for cats and non-human primates in some countries (Selmi *et al* .,2004; Kistner, 2018). However, because it is associated with increased muscle tone, involuntary movement and a high incidence of excitation during recovery, it is usually combined with a tranquilizer or sedative. (Clarke *et al* ., 2014; Berry. 2015; Kistner, 2018).

Ketamine combination with α2-adrenoceptor agonists for anesthesia in cats is well established (Selmi *et al* ., 2003; Thomas and Lerche, 2011; Clarke *et al* ., 2014). Dexmedetomidine, the active enantiomer of medetomidine, is the latest α2 agonist sedative. It is reportedly twice as potent as medetomidine, more selective for α2- receptors than xylazine and thus has fewer side effects (Ansah *et al* ., 1988; Kuusela *et al* ., 2000; Thomas and Lerche, 2011; Carvahalo *et al* ., 2019). Dexmedetomidine compensates for the poor muscle relaxant and analgesic effects of ketamine, while the cardiac stimulating properties of ketamine partially compensate the dexmedetomidine-induced bradycardia (Haskins *et al* ., 1986; Verstegen *et al* ., 1988). Both dexmedetomidine and ketamine can be administered subcutaneously, intravenously and intramuscularly, thus making the combination useful in feline practice for procedural sedation and anaesthesia especially for difficult to handle or feral cats using the intramuscular route (Clarke *et al* ., 2014; Kistner, 2018).

A cat under dexmedetomidine - ketamine anaesthesia may need to be administered a diuretic for various reasons. Cats are small in size and prone to fluid overload which may need to be treated with a diuretic. Also, a cat on furosemide for congestive heart failure may require ketamine anaesthesia.

In cats, ketamine is predominantly excreted as an unchanged metabolite and directly excreted by the kidney (Berry, 2015). In most other species, metabolism of ketamine occurs in the liver. It is demethylated by hepatic microsomal enzymes, reducing the active metabolite norketamine. Norketamine is hydroxylated and then conjugated to form water-soluble and inactive glucuronide metabolites that are excreted by the kidney (Stoelting, 1999). In cat, however, ketamine is biotransformed by hepatic microsomal enzymes to norketamine, which is

excreted unchanged in the urine (Hanna *et al* ., 1988; Berry, 2015; Kistner, 2018). Possible drug interaction may therefore be expected when a diuretic and dexmedetomidine - ketamine combination is administered. A few studies have investigated drug-drug interactions between diazepam-ketamine and xylazine- ketamine anaesthesia and furosemide in both cats and rabbits with varying results (Adetunji *et al* ., 2010; 2013). There is, however, a paucity of information in literature, on furosemide concurrent administration during dexmedetomidine-ketamine anaesthesia in cats. The aim of this study, therefore, was to evaluate the effects of furosemide on dexmedetomidine-ketamine anaesthesia in cats.

MATERIALS AND METHODS

Animals: Five adult domesticated, home-bred, short-haired intact local cats (2 females and 3 males) acquired from a local market in Ibadan, Nigeria, mean body weight ± SD of 1.59 ± 0.0kg were studied.

Animal Housing: The cats were housed at animal house (Cat section) of the Veterinary Surgery and Radiology Department, University of Ibadan, in clean, well aerated compartments and with beddings and sand boxes.

Animal Stabilization: The cats were acclimatized for a period of 4 weeks in order to get them adjusted to the new environment, feeding regime and handling. The cats were given oral anthelminthic, pyrantel pamoate (Pyranthrin®, Neimeth pharmaceuticals, Oregun, Nigeria) supplied as 250mg/ml suspension at a dosage of 5mg/kg body weight. They were fed with home-made food comprising fish, commercial cat food (Binggo®, Grand Cereals, Nigeria) egg, rice, solid pap and palm-oil twice daily and water was provided ad-libitum. Just before the commencement of the experiments they were judged to be in good health based on result of comprehensive clinical examination.

Trial Drugs: The experimental drugs were-

1) Furosemide (Lasix®, Philomide), supplied as a 10mg/ml solution for intramuscular or intravenous injection in a 2 ml ampoule.
2) Dexmedetomidine (Dexdomitor®; Orion Corporation, Orionintie 1 FI-02200 Espoo, Finland) supplied as a 0.1mg/ml solution for intramuscular or intravenous injection in a 15-ml multi dose vial.
3) Ketamine hydrochloride (Ketalar®; Kwality Pharmaceuticals Pvt. Ltd, Amritsar-India) was supplied as a 50mg /ml aqueous solution for intramuscular or intravenous injection in a 10-ml multi-dose vial.

The drugs were administered with 1ml or 2ml syringe.

Study design: The cats (3 males and 2 female) were employed in the two set of trials at one-week interval. In the first set of trials (DK) dexmedetomidine was administered as a pre-medicant, followed after 10 minutes, by ketamine. In the second trial (DKF), the cats were premedicated with dexmedetomidine followed after 10 minutes by simultaneous administration of ketamine and furosemide. The cats' physiological parameters were taken every 10 minutes for 60 minutes. Selected anaesthetic indices were recorded.

Trial drugs administration and monitoring: Food was withheld from the cats 12 hours prior to drug administration, but they were allowed free access to water. The cats body weights were then determined using a weighing scale (Camry scales, China). The DK group had an intramuscular injection of 10 mcg/kg followed ten minutes later with intramuscular administration of ketamine at a dosage of 10 mg / kg. After 7days (allowance for wash-off), the second trial (DKF) commenced with intramuscular injection of dexmedetomidine (10 mcg/kg), followed 10 minutes later with intramuscular administration of ketamine and furosemide at the dose rate of 10mg/kg and 2.5mg/ kg respectively.

Following loss of righting reflex, each cat was placed on lateral recumbency and allowed to breathe in-room air for the duration of the study. A pedal withdrawal reflex following paw-pinch with artery forceps applied at interdigital skin and closed at the third ratchet was used to evaluate loss of pain sensation. The evaluation was done immediately after ketamine administration and repeated at two-minute intervals until the pedal withdrawal reflex reappeared.

Measurements of physiological variables: Following the loss of righting reflex by the cats the heart rate (HR), respiratory rate (RR) and rectal temperature (RT) were determined and thereafter at 10 minutes' interval over a 60-minute period. The heart rate (in beats per minute) was determined with the aid of a precordial stethoscope. Respiratory rate (in breaths per minute) was determined by counting the cat's chest movement while rectal temperature (in °C) was determined using a mercury-in- glass clinical thermometer.

Calculations: The following anaesthetic indices were calculated:

a) Onset of anaesthesia: time interval (in minutes) between ketamine administration to loss of righting reflex.
b) Duration of analgesia: time interval (in minutes) between loss of pedal reflex and return of pedal reflex.
c) Duration of recumbency: time interval (in minutes) between loss of righting reflex and assumption of sternal posture.
d) Time to standing: time interval (in minutes) between assumption of sternal posture and time to stand.

Statistical analysis:

All data were expressed as means ± standard deviation (SD). The means of the anaesthetic indices between the DK and DKF groups were compared using student's t-test for paired data. The respective means of the HR, RR and RT were compared using analysis of variance for repeated measures followed as appropriate by Tukey-Kramer multiple comparisons test (Dawson and Trapp, 2004). A p-value of less than 0.05 was accepted for statistical significance in all comparisons.

RESULTS

Observation: All the cats reacted to pain on intramuscular injection of the drugs. Two cats, one each in the Dexmedetomidine/Ketamine (DK) and

Dexmedetomidine/Ketamine/Furosemide (DKF) groups defecated some minutes after ketamine administration. Salivation was observed in two cats in the (DK) group. In the (DKF) group, a cat salivated while two others vomited.

Anesthetic indices: The selected anesthetic indices that were calculated are shown in Table 1. Time to onset of anaesthesia in the cats with DK (2.4 ± 1.14 min) was similar to that with DKF (2.2±0.45 min) (p = 0.729). The duration of analgesia with (DK) 31.8 ± 14.31 min was not significantly different (p = 0. 247) from that with DKF (42.6±13.01 min). The duration of recumbency with DKF, though longer, (71.60±17.94 min) but not significantly different from that with DK (51.20±16.24 min) with a p-value of 0.096. Time to standing was shorter with DKF (3.6±2.80 min), but was not significantly different when compared with DK (8.0±3.81 min) (p = 0.073).

Table1:
Showing selected anesthetic indices of the intramuscular administration of dexmedetomidine/ketamine and dexmedetomidine/ketamine /furosemide in cats studied.

Treatment groups	Anaesthetic Indices (min)	
	D-K[a]	D-K-F[b]
Onset of Anaesthesia	2.4 ±1.14	2.2 ± 0.45
Duration of Analgesia	31.8 ±14.31	42.6±13.01
Duration of Recumbency	51.2 ± 16.24	71.6 ±17.94
Time to Standing	8.0 ± 3.81	3.6 ±2.80

Data are expressed as means ± standard deviation
*a) **DK**: Dexmedetomidine/Ketamine group (10mcg/kg of dexmedetomidine-10mg/kg of ketamine)*
*b) **DKF:** Dexmedetomidine/Ketamine/Furosemide group (10mcg/kg of dexmedetomidine-10mg / kg of ketamine-2.5mg/kg of furosemide*)

Physiological parameters
The mean heart rate, respiratory rate and temperature of the cats following the intramuscular administration of DK and DKF are shown in Table 2.
Heart rates: Mean heart rates with DK ranged from 96.0±19.39 to 112.8±44.3 beats/min while that of DKF ranged between 84.8±8.67 and 113.2 ±30.71 beats/min. There was no significant difference (p between the two groups.
*Respiratory rate***:** Mean respiratory rates of the group DK ranged from 24.8±19.1 to 71.2 ±34.3 breaths/min while that of DKF ranged from 17.4 ±6.15 to 48.8 ± 12.13 breaths/min. Although there was no significant difference (p>0.05) in the respiratory rates between the two treatments, the values were generally lower in the DKF group.
*Rectal temperature***:** Mean rectal temperatures with DK ranged between 35.1±1.24 and 37.62 ±0.75°C and 36.0 ± 0.54 to 37.64± 0.63°C with DKF. There were no significant differences in mean RT between the two groups(p>0.05) though values fell from the 40th minute of anaesthesia.

DISCUSSION

The observed vomiting by two cats following DKF administration was consistent with emetic effect of alpha 2 agonists in this species (Granholm, 2006, 2007; Thomas and Lerche; 2011; Robertson *et al* ., 2018; Carvahalo *et al* ., 2019). Many cats vomit following administration of dexmedetomidine especially with high doses (Robertson *et al* ., 2018). The dose rates of both dexmedetomidine and ketamine used in this study were those recommended in literature (Neto, 2009). However, dexmedetomidine is associated with fewer side effects than the older α2 agonist, xylazine (Thomas and Lerche,2011). Salivation was also reported in cats given dexmedetomidine- ketamine combination (Carvahalo *et al* ., 2019). Salivation in some of the cats in our study may therefore not be attributable to ketamine alone (Clarke *et al* ., 2014; Thomas and Lerche, 2011) but to both ketamine and dexmedetomidine effects. Anticholinergic (atropine) is useful in preventing or treating older α2 agonist associated salivation in dogs, but it's use in cats is associated with the production of thick mucous secretions within the airways and this viscous secretion may predispose the patient to airway blockage (Thomas and Lerche, 2011). Furthermore, anticholinergics may elicit prolonged tachycardia with α2-agonist – ketamine combinations (Alvaides *et al* ., 2008; Thomas and Lerche, 2011). Routine anticholinergic administration to prevent dexmedetomidine induced bradyarrhythmias is also contraindicated because it can cause significant hypertension (Montero *et al* ., 2009) and may be associated with premature ventricular depolarizations (Alvaides *et al* ., 2008). Both dexmedetomidine and ketamine cause pain on intramuscular injection as observed in these cats (Thomas and Lerche, 2011). The result of this study showed similar anaesthetic induction times in the cats to DK (2.4± 1.14 min) and DKF (2.2 ± 0.45min). Similar studies in rabbits with xylazine- ketamine, and in cats with diazepam/xylazine-ketamine (Adetunji *et al* ., 2010, 2013) also reported that administration of furosemide with the sedative- ketamine combinations did not have any influence on anaesthetic induction times.

Table 2:
Showing the heart rate, respiratory rate and rectal temperature responses of the cats to intramuscular administration of dexmedetomidine-ketamine alone (DK) and dexmedetomidine-ketamine-furosemide (DKF).

Time interval	HR(beats/min)		RR (breaths/min)		RT(^{0}C)	
(min)	DK	DKF	DK	DKF	DK	DKF
0[a]	100.4±38.5	112.2±11.3	40.9±23.3	48.8±12.1	37.0±0.7	37.5±0.9
10	111.6±28.8	109.0±5.7	28.8±27.3	17.4±6.2	37.6±0.7	37.6±0.6
20	96.0±19.4	89.0±11.5	24.8±19.1	19.8±6.7	37.5±0.9	37.0±0.6
30	97.6±2.9	84.8±8.7	36.4±27.6	29.2±10.0	37.9±1.4	37.0±0.6
40	112.8±44.3	87.2±14.8	36.8±27.6	36.8±17.3	36.1±1.4	36.0±0.5
50	105.5±28.1	94.0±26.1	39.6±25.4	34.0±13.3	36.6±1.2	36.8±0.6
60	110.4±32.9	87.0±14.5	71.2±34.3	48.4±15.0	35.1±1.2	36.4±0.6

Data were expressed as means ± SD

Nonetheless, the concurrent administration of furosemide to the dexmedetomidine- ketamine anaesthetic combination produced longer duration of analgesia (DKF- 42.6 ± 13.01 min; DK- 31.8±14.31min) and recumbency (DKF- 71.6 ± 17.94 min; DK- 51.2±16.24 min) but a shorter standing time (DKF- 3.6 ± 2.8 min; DK- 8.0±3.81min) than dexmedetomidine-ketamine alone (Table 1). The greater duration of recumbency associated with the DKF group than the DK values in this study is consistent with the findings of Hanna and others (1988) who reported that, on the basis of measured pharmacokinetic parameters, the concurrent use of diuretics such as furosemide prolonged the renal excretion of ketamine in cats. In a similar study in rabbits, inclusion of furosemide with xylazine-ketamine anaesthetic combination also produced a longer duration of recumbency (Adetunji *et al* ., 2013). In addition, the duration of recumbency of 51.2±16.24 min obtained for the DK is similar to 51.6 ±13.5 min recorded following administration of dexmedetomidine-ketamine combination in cats by Selmi and others (2003).

The heart rates obtained from the cats with both DK and DKF treatments did not show any significant differences ($p > 0.05$) although the DKF (84.8±8.67 and 113.2 ±30.71 beats/min) values were generally lower than the values for DK (96.0±19.39 to 112.8±44.3 beats/min) (Table 2). Acceptable heart rate of cats under general anaesthesia is about 100 beats/minute (McKelvey and Hollingshead, 2000; Kennedy and Johnson, 2015) although values of 60-120 beats/min are usually seen (McKelvey and Hollingshead, 2000). Whereas α2-agonists are known to produce bradycardia, ketamine stimulates the cardiovascular system (Kistner, 2018). The possibility of ketamine partially counteracting the α2 adrenoceptor agonist-induced bradycardia and hypotension has been suggested (Haskins, 1988; Verstegen, 1991). The lowest heart rates recorded following both DK and DKF treatments were close to 88 beats/min obtained in a similar study (Selmi *et al* ., 2003). The administered a2-agonists alone produced a minimal respiratory effect in healthy dogs and cats, characterized by a decrease or no change in respiratory rate and minimal blood gas tension (Berry, 2015). However, significant hypoventilation resulting in hypoxia can occur when a2-agonists are administered with other drugs like opioids, ketamine or propofol (McDonnel and Kerr, 2007). The respiratory rates with both treatments in this study (Table 2) were consistent with possible rates of up to 50 breaths/minute especially with moderate anaesthetic depth (Mckelvey and Hollingshead, 2000).

The mean rectal temperatures obtained following both DK and DKF treatments were similar (Table 2) and fell within the normal temperature range of 36.7- 38.9°C in cats (Levy *et al* ., 2015) until the 60th minute in DK treatment when the cats became hypothermic (35.1±1.24°C; Table 2). It is therefore suggested that warming devices to treat hypothermia should be made available with the use of this combination.

It was concluded that concurrent administration of furosemide with dexmedetomidine- anaesthesia in cats prolonged the duration of analgesia and recumbency but had no effect on onset of anaesthesia. A cat on this anaesthetic combination concurrently placed on furosemide medication will therefore need to be carefully monitored until full recovery.

REFERENCES

Adetunji, A., Lawal, F. M. and Oguntoye, C. O. (2013). The effect of concurrent administration of furosemide on xylazine/ketamine anaesthesia in rabbits. NVJ. 34 (4): 863-869.

Adetunji, A., Oguntoye, C. O., Lawal, F.M. and Thani, V. O. (2010). The effect of concurrent administration of furosemide on diazepam/ketamine anaesthesia in cats. In: Proceedings of the 47th Annual Congress of the Nigerian Veterinary Medical Association. 70 -73.

Alvaides R. K., Teixeira Neto, F. J., Aguiar, A. J. A. and Steagall, P. V. (2008). Effects of acepromazine or atropine given before dexmedetomidine in dogs. Vet. Rec. 162 (10) :852-856. and Physiology in Anesthetic Practice, 3rd edn. Williams & Wilkins, Philadelphia: Lippincott, pp 140–157.

Ansah, O. B., Raekallio, M. and Vainio, O. (1998). Comparison of three doses of dexmedetomidine with medetomidine in cats following intramuscular administration. J. Vet. Pharmacol. Ther. 21: 380–387.

Berry, S. H. (2015). Injectable anaesthetics. In: Tranquilli, W. J., Thurmon, J. C. and Grimm, K. A. (eds.) Lumb and Jones' Veterinary Anesthesia and Analgesia. 4th edn. Blackwell, Ames, Iowa, U.S.A., pp 297-331.

Carvalho, E. R., Champion, T., Vilani, R. G. O. C., Freitas, G. C., Ambrosini, F., Silva, G. A., Gonçalves, K. S. and Fischborn, J. C. J. (2019). Sedative and electrocardiographic effects of low dose dexmedetomidine in healthy cats. Pesq. Vet. Bras. 39 (2):142-147.

Clarke, K. W., Trim, C. M. and Hall, L. W. (2014). General Pharmacology of the injectable agents. In: Clarke, K. W., Trim, C. M. and Hall, L. W. Veterinary Anaesthesia. Saunders Elsevier Ltd., London, pp135-148.

Dawson, B. and Trapps, R. G. (2004). Basic and clinical biostatistics, 4th edition, McGraw Hill, New York, pp 162-189.

Granholm, M., McKusick, B. C., Westerholm, F. C. and Aspegrén, J. C. (2006). Evaluation of the clinical efficacy and safety of dexmedetomidine or medetomidine in cats and their reversal with atipamezole. Vet. Anaesth. Analg. 33(4): 214-223.

Granholm, M., McKusick, B. C., Westerholm, F. C. and Aspergen, J. C. (2007) Evaluation of the clinical efficacy and safety of intramuscular and intravenous doses of dexmedetomidine and medetomidine in dogs and their reversal with atipamezole. Vet. Rec. 160 (26):891-897.

Hanna, R. M., Borchard, R. E. and Schmidt, S. L. (1988). Pharmacokinetics of ketamine HCl and metabolite I in the cat: a comparison of I.V., I.M., and rectal administration. J. Vet. Pharmacol. Ther. 11(1):84-93.

Haskins, S. C., Patz, J. D., Farver, T. B. (1986). Xylazine and xylazine-ketamine in dogs. Am. J. Vet. Res. 47:636–641.

Kennedy, M. J. and Johnson, R. A. (2015). Dexmedetomidine and Atipamezole Clinician's Brief. 65-67

Kistner, S. B. R. (2018). Injectable anaesthetics. In: Duke-Novakovski, T., Marieke de Vries and Seymour, C. (eds)

BSAVA Manual of Canine and Feline Anaesthesia and Analgesia 3rd Edition British Small Animal Veterinary Association, Quedgeley, Gloucester, pp 190 - 213

Kurdi, M. S., Theerth, K. A. and Deva, R. S. (2014). Ketamine: Current applications in anesthesia, pain, and critical care. Anesth Essays Res. 8(3): 283–290.

Kuusela, E., Raekallio, M. and Vainio, O. (2000). Comparison of three doses of dexmedetomidine and its enantiomers in dogs. J. Vet. Pharmacol. Ther. 23:15–20.

Levy, J. K., Nutt, K. R. and Tucker, S. J. (2015). Reference interval for rectal temperature in healthy confined adult cats. J. Feline Med. Surg. 17(11):950-952.

McDonell, W. N. and Kerr, C. L. (2007). Respiratory system. In: Tranquilli, W. J., Thurmon, J. C. and Grimm, K.A. (eds.) Lumb and Jones' Veterinary Anesthesia and Analgesia. 4th ed. Blackwell, Ames, Iowa, pp 117-152.

McKelvey, D. and Hollingshead, K. W. (2000). General anaesthesia. In: McKelvey, D. and Hollingshead, K.W. (eds.) Veterinary Anesthesia and Analgesia. Mosby, St. Louis. Missouri, pp 51-110.

Mercer, S. J. (2009). 'The Drug of War' – a historical review of the use of Ketamine in military conflicts. J. Roy. Naval Med. Serve. 95: 145–150.

Monteiro, E. R., Campagnol, D., Parrilha, L. R. and Furlan, L. Z. (2009) Evaluation of cardiorespiratory effects of combinations of dexmedetomidine and atropine in cats. J Feline Med. Surg. 11: 783–792.

Neto, F. J. T. (2009). Dexmedetomidine: a new alpha-2 agonist for small animal practice Proceedings of the 34th World Small Animal Veterinary Congress WSAVA 2009, São Paulo, Brazil.

Robertson, S. A., Gogolski, S. M., Pascoe, P., Shafford, H. L., Sager, J. and Griffenhagen, G. M. (2018) J. Feline Med. and Surg. 20: 602–634.

Selmi, A. L., Mendes, G. M., Lins, B.T., Figueiredo, J. P. and Barbudo-Selmi, G. R. (2003). Evaluation of the sedative and cardiorespiratory effects of dexmedetomidine, dexmedetomidine-butorphanol and dexmedetomidine-ketamine in cats. J. Am. Vet. Med. Assoc. 222:37–41.

Selmi, A. L., Mendes, G. M., Figueiredo, J. P., Barbudo-Selmi., G. R. and Lins, B. T. (2004). Comparison of medetomidine-ketamine and dexmedetomidine-ketamine anesthesia in golden-headed lion tamarins. Can. Vet. J. 45: 481-485.

Stoelting R. K. (1999). Non barbiturate induction drugs. In: Stoelting, R. K. (ed.) Pharmacology, Thomas, J. A. and Lerche, P. (2011): Anesthetic agents and adjuncts. In: Anesthesia and Analgesia for Veterinary Technicians 4th Edn Mosby Elsevier, Missouri, USA, pp 50 -95.

Verstegen J., Fargetton X., Ectors F. (1989) Medetomidine-ketamine anaesthesia in cats. Acta Vet Scand; 85:117–123.

Verstegen J., Fargetton X., Donnay I., Ectors F. (1991): An evaluation of medetomidine/ketamine and other drug combinations for anaesthesia in cats. Vet. Rec. 128 (2) :32–35.