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Anaesthetic efficacy of xylazine-ketamine-butorphanol and dexmedetomidine-ketamine-butorphanol combination for ovariohysterectomy in cat

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The study was conducted to compare the anaesthetic efficacy of xylazine-ketamine-butorphanol and dexmedetomidine-ketamine-butorphanol combinations for ovariohysterectomy in cats. Twelve healthy cats brought for ovariohysterectomy were randomly divided in two groups, in one group dexmedetomidine-ketamine-butorphanol and in another group xylazine-ketamine-butorphanol were used to induce anaesthesia. The animals were assessed based on different clinical, physiological and biochemical parameters recorded before induction, at induction and after recovery from anaesthesia. The cats administered with dexmedetomidine-ketamine-butorphanol combination exhibited a better quality of anaesthesia, a shorter induction time and recovery time. A significant variation was observed in clinico-physiological parameters after anaesthetic induction in both the combinations. A non-significant variation in the values of haematological and biochemical parameters was observed in both groups for the duration of anaesthesia. It can be concluded that the combination of dexmedetomidine-ketamine-butorphanol offered superior anaesthetic quality with smooth induction and faster recovery for ovariohysterectomy in cats, compared to the use of xylazine-ketamine-butorphanol.

Key words: *Anaesthesia, Cat, Dexmedetomidine, Ovariohysterectomy*

Cat population has been increasing significantly over the past few years due the popularity in cats being kept as pets as well due to increase in stray cats. With increasing populations, birth control measures like surgical sterilization have become the need of the hour. Potential benefits of sterilization include population control, prevention of diseases of the reproductive tract, and elimination of undesirable behaviours associated with hormonal cycling (DeTora and McCarthy, 2011). Ovariohysterectomy is a surgical procedure consisting of laparotomy with ablation of both ovaries and the uterus (Bencharif *et al.*, 2010). In bellicose animals like cats, surgical interventions necessitate a sufficient anaesthesia with adequate sedation and postoperative pain control while minimizing the risk of overdosing (Lee *et al.*, 2016).

Currently, intramuscular injections are administered to sedate cats undergoing spay surgeries. This is followed by establishing intravenous access to facilitate induction, endotracheal intubation, and the maintenance of anaesthesia through periodic injections of anaesthetic boluses or the use of gaseous anaesthesia. It is necessary to create and standardize balanced anaesthetic protocols in order to reduce the need for manual restraint and to provide the effects of general anaesthesia with a single injection prick. Administering a single injection that includes sedative, analgesic and anaesthetic induction agents substantially reduces patient pain and stress; thus, combining premedication and anaesthetic induction agents in a single injection was advised (Fazio *et al.*, 2015). A combination of alpha-2-adrenergic agonist, a dissociative anaesthetic and opioid analgesic provides balanced anaesthesia in a single intramuscular injection. The objective of this research was to establish a safe and potent single administration protocol by comparing the sedative effects of the two combinations: xylazine-ketamine-butorphanol and dexmedetomidine-ketamine-butorphanol administered intramuscularly for ovariohysterectomy in cats.

Materials and Methods

The current investigation involved 12 healthy female cats which were presented for ovariohysterectomy. The cats were randomly categorized into two groups, comprising of 6 animals, notwithstanding the breed, age and weight. All the cats included in the study were subjected to physiological, haematological and biochemical examination before undertaking the surgical procedure to detect any latent pathological condition and were assessed for the quality of anaesthesia.

In all the animals, premedication was done by administering meloxicam (0.1 mg/kg body wt), chlorpheniramine maleate (0.5 mg/kg body wt) and amoxicillin sodium and sulbactam sodium (12.5 mg/kg body wt) administered intramuscularly. The

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anaesthesia was induced in group I cats using xylazine-ketamine-butorphanol (XKB) combination (X=1 mg/kg, K=10 mg/kg, B=0.2 mg/kg body wt); and in group II, the induction of anaesthesia was achieved using and dexmedetomidine-ketamine-butorphanol (DKB) combination (D=25 µg/kg, K=10 mg/kg, B=0.2 mg/kg body wt) administered intramuscularly. The cats were intubated and oxygenated @ 0.5 L/min. The extent of anaesthetic depth achieved by the two protocols were assessed by observing the ear flicker response, mandibular muscle tone, palpebral reflex, eyeball position and pedal reflex, which were recorded at induction and were graded accordingly. Degree of muscle relaxation was judged on the basis of extent of exteriorization of the suspensory ligament and mandibular muscle tone. Degree of analgesia was judged based on response to incision and stretching of suspensory ligament. Ovariohysterectomy was performed by midline laparotomy. Anaesthesia was also assessed on the basis of induction time, anaesthetic duration and recovery time. Clinico-physiological parameters like rectal temperature, heart rate and respiratory rate and haemato-biochemical parameters like Hb, PCV, TEC, total protein, ALP, AST and ALT were recorded before induction, at induction and after recovery. Ovariohysterectomy was performed by midline celiotomy approach. Data gathered for this study was statistically analyzed using ICAR WASP 2.0 software's Two-Way Factorial Experimental Design and Two Sample t-test.

Results and Discussion

Ear flicker reflex did not exhibit a significant difference between groups and it vanished completely at the time of induction (Table 1). Palpebral reflex was moderate and manifested as twitching of eyelid muscles in three cats from group I and four cats from group II. Pedal reflex was absent in all the cats. No response to the incision was elicited by any cat included in both groups. This may be attributed to the visceral analgesic properties of alpha-2-adrenergic agonists and dissociative anaesthetic ketamine, along with the opioid analgesic butorphanol. A cumulative effect of these three drugs when administered together resulted in profound analgesia due to inhibition of transmission, modulation and perception of pain. Mandibular muscle tone was observed to be relaxed in all the cats except in one case in group I. Group II animals had superior mandibular muscle tone relaxation in comparison to group I. This could be due to the fact that dexmedetomidine is more potent than xylazine. Eyeball was observed to be centrally placed in all the cats after anaesthetic induction. Adequate muscle relaxation was observed in 5 cats each from group I and group II, whereas one cat each from both groups exhibited inadequate muscle relaxation (mild degree). Adequacy of muscle relaxation was determined on the basis of abdominal muscle tension after incision and extent of stretching of ovarian suspensory ligament. These findings on quality of anaesthesia are in accordance with the results observed by Sodagar *et al.* (2021).

Mean induction time in animals of group I (10.16±1.01 min) and in group II (6.83±0.65 min) differed significantly. This might be attributed to more potency of the α-2-adrenergic agonist dexmedetomidine. Induction was smooth, rapid and free from excitement in both the anaesthetic combinations, as also reported in earlier studies (Volpato *et al.*, 2014; Sodagar *et al.*, 2021). The mean duration of anaesthesia in group I was 45.83±8.5 min and in group II it was 56.5±1.60 min. Duration of anaesthesia was significantly ($P<0.05$) longer in group II as compared to group I, which could be attributed to the enhanced specificity of dexmedetomidine towards the alpha-2 adrenergic receptors as compared to xylazine. The time required to recovery from anaesthesia was significantly ($P>0.05$) longer in

Table 1: Evaluation of body reflexes to assess quality of anaesthesia in group I and II.

Groups	**I**		**II**	
Reflexes	**No. of cats**	**Score**	**No. of cats**	**Score**
Ear flicker reflex	5	1	5	0
	1	0	1	1
Palpebral reflex	3	2	4	1
	3	1	2	2
Pedal reflex	6	0	6	0
Mandibular muscle tone	5	Relaxed	6	Relaxed
	1	Slightly tense		
Position of eyeball	6	Centrally placed	6	Centrally placed
Muscle relaxation	5	Adequate	5	Adequate
	1	Inadequate	1	Inadequate
Degree of analgesia	4	No response	5	No response
	2	Slight movement	1	Slight movement

the cats of group I (64.5±4.71 min) as compared to group II (54.16±3.51 min). The extended recovery duration linked with XKB anesthesia, in contrast to DKB anesthesia, may be attributed to the administration of a lower dose of dexmedetomidine (25 mcg/kg) compared to the manufacturer's recommended dosage of 45 mcg/kg. Meanwhile, the optimal recommended dose of xylazine (1 mg/kg) was utilized in the anaesthetic combination. The findings on duration of anaesthesia were in contrast with the observations reported by Ko and associates (2011), they stated that additional supplementation of anaesthetic drug might be required to perform surgeries that last for a longer duration. The animals recovered from anaesthesia smoothly without any sign of excitement with both anaesthetic protocols, as also reported in earlier studies (Cistola *et al.* 2004; Ko *et al.*, 2011; Sabek *et al.*, 2021; Pal *et al.*, 2022).

The mean value of rectal temperature (RT) in both groups showed decreasing trend at induction and further decline during recovery from anaesthesia (Table 2). The gradual decline in RT at induction could be attributed to the peripheral vasodilation eventually leading to increased heat loss caused by the action of alpha-2-adrenergic agonists, xylazine and dexmedetomidine. Impaired thermoregulation due to drug administration causing muscle relaxation, prevention of shivering and a cool ambient temperature can make sedated and anaesthetized patients hypothermic. Similar results on RT following anaesthesia were reported by Cruz *et al.* (2000), Cistola *et al.* (2004), Harrison *et al.* (2011), McSweeney *et al.* (2012), and Sabek *et al.* (2021). A significant decrease in respiratory rate (RR) was observed in both groups after the administration of anaesthetic combination. The decrease in RR could be ascribed to the depressant action on the respiratory system caused by the action of alpha-2-agonist (xylazine and dexmedetomidine) and dissociative anaesthetic ketamine. In spite of a significant reduction in RR upon induction, the values were within the normal physiological range (despite the depressant effects of xylazine and ketamine), which could be attributed to the non-depressant impact of butorphanol on the sensitivity of the respiratory center. These findings are in accordance with the results obtained by Selmi *et al.* (2003), Chen and Chee (2005), Zilberstein *et al.* (2008), Ko *et al.* (2011) and Sabek *et al.* (2021). The mean values of HR for group I and group II were 125.83±3.76 and 141.72±3.56 per min, respectively; the values were significant different between the groups. This phenomenon could be ascribed to the anxiety and arousal experienced by cats upon entering the hospital setting, as well as the hostile demeanor often displayed by feral cats. The significant

Table 2: Mean±SE of physiological and haemato-biochemical parameters at different time intervals in both groups.

Parameter	Groups	Before induction	At induction	After recovery
RectalTemperature (ºF)	I	102.16±0.47	101.66±0.40	100.46±0.40
	II	101.85±0.45	101.25±0.57	101.05±0.40
Respiration rate (per min)	I	37.16±4.22	21.33±1.96	25±2.46
	II	33.83±1.53	19.83±0.54	24.5±0.34
Heart rate (per min)	I	138.16±4.63	112.33±5.85	127±4.66
	II	148.33±3.07	123±7.43	128.5±7.61
Haemoglobin (%)	I	11.15±0.62	11.03±0.62	11.03±0.62
	II	13.5±0.96	13.5±0.96	13.45±0.95
TEC (m/μL)	I	6.86±0.27	6.78±0.28	6.78±0.28
	II	8.2±0.66	8.06±0.65	8.06±0.65
PCV (%)	I	34.03±1.63	33.86±1.64	33.86±1.64
	II	40.5±2.90	40.41±2.89	40.41±2.89
BUN (mg/dL)	I	37.33±2.76	37.8±2.78	37.93±2.79
	II	35.66±1.66	36.11±0.68	35.89±1.66
Creatinine (mg/dL)	I	1.05±0.13	1.12±0.13	1.17±0.14
	II	1.08±0.10	1.16±0.10	1.17±0.11
Total protein (g/dL)	I	6.66±0.32	6.59±0.31	6.52±0.30
	II	6.68±0.19	6.62±0.19	6.58±0.18
ALP (U/L)	I	54.16±3.34	54.76±3.32	55.16±3.34
	II	54±3.41	54.5±3.41	54.93±3.39
ALT (U/L)	I	57.33±5.30	56.76±5.34	56.58±5.36
	II	66.66±3.24	66.11±3.19	66±3.16
AST (U/L)	I	43±4.51	43.61±4.49	43.9±4.45
	II	44.16±3.15	44.86±3.16	45.21±3.09

decrease in the HR at induction may be attributed to the action of alpha-2 agonist associated phenomena: an increase in arterial blood pressure inducing a baroreceptor-mediated increase in vagal outflow causing bradycardia, or a decrease in sympathetic tone due to dexmedetomidine-mediated decrease in norepinephrine release in the CNS (Santos *et al*., 2010). Dexmedetomidine promotes a biphasic decrease in HR by initially activating peripheral α2-adrenoreceptors, increasing systemic vascular resistance, followed by a longer lasting centrally mediated increase in vagal activity (Cremer and Riccó, 2018). Butorphanol causes a reduction in HR secondary to increased parasympathetic tone. The HR was maintained in the physiological range due to the action of ketamine, which was known to cause tachycardia secondary to increased sympathetic tone. These findings were in similar with the results obtained by Selmi *et al.* (2003), Chen and Chee (2005), Zilberstein *et al.* (2008), Ko *et al.* (2011) and Sabek *et al.* (2021).

The mean values of Hb, TEC, and PCV showed a non-significant decline at the time of induction and remained constant throughout the anaesthetic duration and recovery period (Table 2). The insignificant decrease in the values of Hb, TEC, and PCV could be because of pooling of blood cells in spleen and other reservoirs as a result of diminished sympathetic activity. There was a non-significant decrease in the values of total protein at induction as compared to the base values observed before induction, which might be attributed to a dilution effect associated with intercompartmental fluid shifting. There are concerns about the adequacy of tissue perfusion following alpha-2-agonists due to increased vascular resistance. A non-significant increase in the mean values of creatinine was observed at induction as compared to the base value. There was no significant variation in the mean values of creatinine, BUN, ALP, ALT and AST, when compared between the groups, and the values were within the normal range (Table 2). The rise in creatinine and BUN levels observed during anesthesia may be attributed to heightened hepatic urea synthesis stemming from amino acid degradation (Verma *et al*., 2018) or it might be ascribed to the transient inhibitory impact of anaesthetic agents on renal blood flow, leading to a decline in glomerular filtration rate (Saikia *et al*., 2016). The increase in the levels of alkaline phosphatase, alanine amino transferase and aspartate amino transferase, could be attributed to a changes in liver metabolism as a result of altered hepatic blood flow due to anaesthetic effect (Cheung *et al.,* 2017). It may also be attributed to the alteration in cell membrane permeability in response to haemodynamic changes by the anaesthetic agents. This indicated the probable leakage of these enzymes through plasma membrane of hepatic cells rather than release from the damaged cells (Tandekar, 2009).

It can be concluded that the combination of dexmedetomidine-ketamine-butorphanol offered superior anaesthetic quality with smooth induction and faster recovery for ovariohysterectomy in cats, as compared to the use of xylazine-ketamine-butorphanol combination.

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