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Evaluation of Xylazine and Acepromazine as Premedicants to Ketamine Anaesthesia in Dogs Insufflated with CO_2 during Laparoscopic Vasectomy

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ABSTRACT

The study was conducted to evaluate and compare atropine-xylazine-ketamine and atropine-acepromazine-ketamine anaesthetic protocol in twelve healthy dogs undergoing laparoscopic vasectomy following 12 mmHg CO_2 insufflation. Three port entries were used for performing laparoscopic vasectomy. Monopolar electrocautery was used for coagulation and cutting of a 2-3 cm piece of vas deferens. Anaesthetic and physiological parameters were recorded at 0 minutes (before administration of any drug), 10 minutes after administration of ketamine, 30 minutes after insufflation of abdominal cavity, and 60 minutes after desufflation in both the groups. Pneumoperitoneum with CO_2 to an intra-abdominal pressure of 12 mmHg did not have any significant effects on physiological, haemato-biochemical and haemo-dynamic parameters and ECG. Surgical plane of anaesthesia with good analgesia and muscle relaxation, smooth induction and recovery was achieved with atropine-xylazine-ketamine combination. Atropine-acepromazine-ketamine combination failed to induce and maintain surgical plane of anaesthesia.

Keywords: Acepromazine, dogs, ketamine, laparoscopy, vasectomy, xylazine

Laparoscopy, also called minimally invasive surgery (MIS), band aid surgery, keyhole surgery, is a modern surgical technique designed for the visual inspection of peritoneal cavity, biopsy of internal organs and various operative procedures in the abdominal and pelvic cavities. During last two decades laparoscopy has been increasingly used for diagnostic as well as many surgical procedures in veterinary patients.

Laparoscopic surgery requires creation of pneumoperitoneum to provide surgical field, allowing visibility and performance of surgical manoeuvres (Hewitt *et al.*, 2007). Appropriate selection of anaesthetic technique and monitoring facilitate surgery and allow early detection and reduction of complications during laparoscopy. Care in selection of an agent for safe anaesthetic management is essential, since it always constitutes a threat to the life of the patient (Orkin and Cooperman, 1983). This becomes more important during laparoscopic surgery due to the added cardiopulmonary effects of pneumoperitoneum.

Different anaesthetic combinations have been used considering their efficiency and non-toxic effects, yet no systematic research has been carried out to evaluate the safety of using different anaesthetic drugs during laparoscopy in animals. The study was conducted to evaluate and compare the atropine, xylazine and ketamine anaesthetic protocol with that of atropine, acepromazine and ketamine in dogs undergoing laparoscopic vasectomy following CO_2 insufflation.

MATERIALS AND METHODS

The study was conducted on twelve healthy male dogs, weighing 12-20 kg, randomly divided into two groups, group A and group B, comprising of six animals each. On the day of surgery, the physiological, haemato-biochemical parameters and ECG (electrocardiography) were recorded. Animals of group A were premedicated with atropine sulfate @ 0.04 mg/kg body weight, followed 20 minutes (min) later by xylazine hydrochloride @ 2 mg/kg body

weight. Ketamine hydrochloride @ 10 mg/kg body weight was administered five min after xylazine. Animals of group B were administered acepromazine maleate @ 0.1 mg/kg body weight 20 min after premedication with atropine @ 0.04 mg/kg. Ketamine was administered @10mg/kg body weight 30 min after injection of acepromazine. All drugs in both the groups were administered intramuscularly. Laparoscopy was performed using standard procedure after insufflating peritoneal cavity with CO_2 to a pressure of 12 mmHg (Ritcher, 2001). The following parameters were recorded at 0 min (before administration of any drug), 10 min after administration of ketamine, 30 min after insufflation and 60 min after desufflation in both the groups.

Anaesthetic parameters

The reflexes were observed every 30 seconds following administration of ketamine till complete induction and each observation was accorded a score from 0 to 3 as shown in Table 1. Relaxation of the jaw was taken as a measure of muscle relaxation during the study and was evaluated by observing the resistance to opening of the jaws and a score was given. Palpebral reflex was recorded as a measure of depth of sedation and was assessed by observing a blink of the eyelids on touching the area around medial canthus of the eyes with index finger. Pedal reflex status was recorded as a measure of depth of analgesia and was assessed by observing the withdrawal reflex to the pinching of inter digital skin of a hind foot of the animal. Response to intubation was recorded to assess the status of laryngeal and swallowing reflexes and feasibility of intubation before beginning insufflation. The response to intubation was recorded by attempting intubation only after the jaw relaxation score was 2 or 3.

Physiological parameters

Heart rate (HR), respiratory rate (RR) and rectal temperature (RT) were recorded as per the standard procedure.

Central venous pressure and Mean arterial pressure

Central venous pressure (CVP) and mean arterial pressure (MAP) were recorded after catheterization of the jugular vein and the carotid artery, respectively. CVP and MAP were recorded before administration of any drug (0 min), 20 min after administration of atropine, 5 min after xylazine, 30 min after acepromazine, 10 min after administration of ketamine, 30 min after insufflation of abdominal cavity, and 60 min after desufflation. All the readings were taken while the animals were in right lateral recumbency.

Electrocardiography (ECG)

ECG was recorded using standard bipolar limb lead II system, before administration of any drug (0 min), 20 min after administration of atropine, 5 min after xylazine, 30 min after acepromazine, 10 min after administration of ketamine, 30 min after insufflation of abdominal cavity and 60 min after desufflation and interpreted for rhythm, time, and voltage.

Table 1: Subjective observations of various reflexes/parameters assessed on the basis of scoring system **(**Ahmad *et al.*, 2011**)**

Reflex/parameter	Score 0	Score 1	Score 2	Score 3
Jaw relaxation	Not allowing to open the jaws	Resistant to opening the jaws and closed quickly	Less resistance to opening the jaws and closed slowly	No resistance and jaw remained open
Pedal reflex	Intact and strong reflex (strong withdrawal)	Intact but weak reflex (animal responding slowly)	Intact but very light reflex (slow and occasional)	Reflex abolished completely
Palpebral reflex	Intact and strong reflex (quick blink)	Intact but weak reflex (slow response)	Very weak reflex (very slow and occasional)	Reflex abolished completely
Response to intubation	Not permitting entry of tube in the mouth	Allowing entry but chewing or coughing	Difficult intubation with coughing	Easy intubation without coughing

Statistical analysis

The data generated was analyzed using Tukey's b test for comparison of the values at different time intervals within the groups and independent samples T test for comparison between the groups at 5% level of significance.

RESULTS AND DISCUSSION

Anaesthetic parameters

The jaws were relaxed completely and could be opened without resistance (score 3) in animals of group A at 3 min after ketamine administration. In group B, jaw relaxation was never complete and score of >2 was never achieved at any time. The pedal reflex was completely abolished (score 3) in group A from 5 min after administration of ketamine, whereas it remained present throughout the period of anaesthesia and did not go beyond the score of 2 at any point of time after administration of ketamine in group B. The palpebral reflex was completely lost (score 3) in the animals of group A at 4 min after ketamine administration and remained absent for 25 min after ketamine administration, however, it remained sluggish throughout the period of anaesthesia in all the animals of group B. Laryngeal and swallowing reflex was abolished (score 3) in animals of group A at 5 min., all the animals could be intubated easily and anaesthesia maintained for 36.75 ± 2.37 min Laryngeal/swallowing reflex was not abolished completely in any animal of group B, and highest score of only 1.55 was achieved till insufflation was started. Intubation was not possible in any animal of group B.

Physiological parameters (Table 2)

The rectal temperature decreased in both the groups at 10 min after administration of ketamine. The decrease was significant ($p<0.05$) in group B. It remained non-significantly below the base value in both the groups at 30 min after insufflation, and in group B even at 60 min after desufflation. There was no significant difference in the rectal temperature between the groups at any time interval. The respiration rate decreased in both the groups and remained significantly lower than the base value at 10 min after ketamine and 30 min after insufflation. However, at 60 min after desufflation the respiratory rate improved approaching the base value in both the groups. The decrease in respiration rate was significantly greater in group B than group A at 10 min after administration of ketamine. The heart rate increased in both the groups 20 min after the administration of atropine and this increase continued even after ketamine administration, the increase being more pronounced in group B. The heart rate started declining by 30 min after insufflation and at 60 min after desufflation the HR was not significantly different from base values. No significant alteration was observed in haemato-biochemical parameters like TLC, DLC, total protein, albumin, Albumin:Globulin, ALT and AST in both the groups throughout the period of observation.

Central venous pressure and Mean arterial pressure (Table 3)

There was a non-significant decrease in CVP throughout the period of anaesthesia when compared with the base

Table 2: Physiological parameters (Mean±SE) of dogs of groups A and B (n= 6)

Parameters (unit)	Group	0 min	10 min after ketamine	30 min after insufflation	60 min after desufflation
Heart rate (beats/ min)	A	88.50 ± 6.91^{a}	$152.33\pm7.33^{b,x}$	$127.00\pm6.78^{a,b,c,x}$	$97.3\pm10.95^{a,c}$
	B	87.33 ± 7.22^{a}	$178.50\pm16.66^{b,y}$	$160.66\pm14.77^{b,c,y}$	$116.6\pm6.89^{a,c}$
Rectal Temp (°F)	A	102.05±0.12	101.58±0.19	101.65±0.12	102.00±0.12
	B	102.0 ± 0.12^{a}	101.02 ± 0.23^{b}	$101.28\pm0.28^{a,b}$	$101.6\pm0.23^{a,b}$
Respiration rate/min	A	21.33 ± 0.88^{a}	$17.00\pm0.36^{b,x}$	17.17 ± 0.25^{b}	19.67 ± 0.33^{a}
	B	21.00 ± 0.73^{a}	$16.00\pm0.25^{b,y}$	17.33 ± 0.22^{b}	20.17 ± 0.54^{a}

Means of a parameter bearing different superscript (a,b,c) in a row or (x,y,z) in a column differ significantly ($p<0.05$)

value in both the groups. The CVP did not return to the pre-anaestheic level even 60 min after desufflation in group A, it showed slight recovery 30 min after insufflation in group B. The difference between the groups at various time intervals was not significant.

The MAP increased non-significantly after administration of atropine in both the groups and it returned to the base value at 30 min after insufflation in group A, however, in group B the MAP after initial rise decreased significantly after the administration of ACP and remained much below the base level even at 60 min after desufflation.

Electrocardiographic parameters (Table 4)

In both the groups, P-wave amplitude showed a non-significant increase 20 min after the administration of atropine. The P-wave duration, in both the groups, remained almost constant throughout the period of anaesthesia. QRS and PR interval did not show any significant alteration in any of the groups.

Surgical plane of anaesthesia with good analgesia and muscle relaxation was achieved in group A. Most of the reflexes were abolished in 5-6 min after ketamine administration and the observations are in agreement with those made by Alkattan and Helal (2013). In spite of the fact that ketamine does not produce muscle relaxation or abolish pharyngeal-laryngeal reflexes, anaesthesia with good muscle relaxation and analgesia produced by the combination in the present study might be due to xylazine which is known to produce reliable dose dependent sedation, analgesia, and muscle relaxation (Lemke, 2007). The duration of anaesthesia, 36.75±2.37 min, was in agreement with the findings of Tiwari *et al.* (1994). Surgical plane of anaesthesia was not achieved in group B probably because acepromazine (ACP) being a tranquilizer

Table 3: MAP and CVP in dogs of groups A and B (n=6)

Parameter	G	0 min before any drug	20 min after atropine	5 min after xylazine and 30 min after ACP	10 min after ketamine	30 min after insuffla.	60 min after desuffla.
MAP	A	88.67±5.10	102.67±6.03	$103.92±13.12^{x}$	$109.17±8.39^{x}$	$89.83±6.49^{x}$	84.17±7.76
	B	$86.25±6.76^{a,b}$	$98.88±6.03^{a}$	$57.25±4.61^{c,y}$	$69.25±4.77^{b,c,y}$	$67.75±4.25^{b,c,y}$	$77.75±4.11^{b,c}$
CVP	A	2.75±1.06	2.00±0.46	0.83±1.35	1.42±1.35	0.43±0.55	0.62±0.23
	B	0.92±1.01	0.66±0.06	-0.77±0.75	-0.60±0.38	-0.08±0.87	-0.08±0.92

Means of a parameter bearing different superscript (a,b,c) in a row or (x,y) in a column differ significantly ($p<0.05$)

Table 4: Various time intervals (durations) and amplitudes on ECG

	Group	0 min	After atropine	After xylazine/ ACP	10 min after ketamine	30 min after insufflation	60 min after desufflation
P amp	A	0.17±0.02	0.20±0.02	0.15±0.01	0.15±0.01	0.18 ±0.02	0.15±0.02
	B	0.18±0.01	0.20±0.02	0.20±0.01	0.21±0.01	0.19 ±0.02	0.20±0.01
P dur	A	0.04±0.00	0.04±0.00	0.04±0.00	0.05±0.00	0.04±0.01	0.03±0.00
	B	0.04±0.00	0.04±0.00	0.05±0.01	0.04±0.00	0.04±0.00	0.04±0.00
QRS com	A	0.05±0.00	0.06±0.01	0.05±0.00	0.05±0.00	0.06±0.01	0.05±0.00
	B	0.06±0.00	0.06±0.01	0.06±0.01	0.06±0.01	0.06±0.00	0.06±0.01
T amp	A	0.25±0.06	0.20±0.05	0.21±0.04	0.18±0.03	0.09±0.01	0.15±0.03
	B	0.33±0.07	0.20±0.05	0.17±0.02	0.13±0.02	0.18±0.03	0.19±0.03
PR int	A	0.12±0.01	0.08±0.01	0.11±0.01	0.15±0.02	0.15±0.03	0.14±0.01
	B	0.14±0.00	0.15±0.01	0.12±0.00	0.12±0.00	0.12±0.00	0.13±0.011

did not produce profound sedation like xylazine and it has no analgesic property. The ACP failed to compensate for the lack of myorelaxant property of ketamine.

Xylazine might be responsible for the non-significant decrease in RT at 10 min following anaesthesia in group A, as $\alpha_2$agonists have been found to activate the hypothalamic alpha-receptors inhibiting the heat conserving mechanism (Ponder and Clarke, 1980). ACP might be responsible for significant decrease in RT partly due to increased heat loss through dilated cutaneous vessels due to α_1-adrenergic block and partly due to depletion of catecholamines in the thermoregulatory center of the hypothalamus that leads to a loss of thermoregulatory control (Lemke, 2007).

Maintenance of HR significantly above the base level in both the groups and its further increase might be due to cardio-stimulatory effects of ketamine mediated through various physiologic mechanisms including sympathomimetic effects, inhibition of intra-neuronal and extra-neuronal uptake of catecholamines. The decrease in RR might be due to direct depressant effect of xylazine in group A and animals receiving acepromazine have been reported to breathe more slowly (Muir *et al*., 1975).

Non-significant decrease in CVP throughout the period of anaesthesia in both the groups could be due to the fact that the animals were kept off water for 6 hours before the trials and were not administered even the maintenance dose of IV fluids. Moreover, high ambient temperature (>40ºC) might have resulted in peripheral vasodilation resulting in slight fall in CVP. In addition, blockade of α_1 adrenergic receptors by ACP in group B leading to vasodilation might be responsible for the fall in CVP (Lemke, 2007). Mild increase in CVP in both the groups following administration of ketamine might be due to the cardio-stimulatory effects of the drug leading to increased cardiac output and systemic vascular resistance (SVR) due to a centrally mediated generalized increase in sympathetic tone (Haskins *et al.*, 1985).

Though xylazine is reported to induce biphasic blood pressure, hypertension followed by hypotension, in dogs, no such change in MAP was observed in the study, probably due to prior administration of atropine which blunted the cardio-vascular effects of xylazine. Moreover, the cardiovascular effects of xylazine after i.m administration have been reported to be less dramatic as compared to i.v. injection (Lemke, 2007). The MAP decreased significantly after the administration of ACP in group B as ACP is known to possess hypotensive properties due to vasodilation. The increase in MAP following ketamine administration in both the groups may be attributed to the cardio-stimulatory effects of ketamine. Insufflation did not appear to have any effect on MAP.

Conclusion: It can be concluded that atropine-xylazine-ketamine provided surgical plane of anaesthesia with prolonged sedation, adequate muscle relaxation, and excellent analgesia and can be safely used for performing laparoscopic procedures in dogs, whereas, atropine-acepromazine-ketamine failed to do so hence, not recommended for laparoscopy. Pneumoperitoneum with CO_2 at an intra-abdominal pressure of 12 mmHg did not have any significant effects on physiological, haemato-biochemical and haemo-dynamic parameters and on ECG.

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