The Haryana Veterinarian (December, 2023) **62(2),** 20-23 ISSN 0033-4359 (P) **Research Article**

EVALUATION OF DOXAPRAM FOR FASTER RECOVERY BEHAVIOUR AND HAEMATO-BIOCHEMICAL PARAMETERS FOLLOWING KETOFOL ANAESTHESIA IN DOGS

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ABSTRACT

The study was conducted on12 clinical cases of female mongrel dogs, randomly divided in two groups which were brought to Department of Veterinary Surgery and Radiology for elective ovariohysterectomy. In both the groups, ketofol continous rate infusion (CRI) was used for the maintenance of anaesthesia. Group A was taken as the control group and in group B, doxapram was administered @ 1mg/kg body weight IV after the completion of ketofol anaesthesia. Anaesthetic recovery and haemato-biochemical parameters were observed during study. A non-significant difference was observed in Hb, TEC, DLC, albumin, BUN, creatinine, ALT and AST values at different time intervals. Comparison within the groups revealed a significant and non-significant decrease in TLC from time interval T1 to T4 in groups A and B, respectively. A significantly lower time was taken for anaesthetic recovery parameters in the doxapram group in comparison to the control group. From the results, it was concluded that doxapram can be used for shortening anaesthetic recovery time in dogs anaesthetized with ketofol CRI without appreciable negative impact on haemato-biochemical parameters.

Keywords: Dog, Doxapram, Ketofol CRI

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The surgical outcome is determined by the patient's condition, the type of operation performed, surgeon skills, anaesthesia and recovery. Recovery is a crucial component of the anaesthetic procedure since it can lead to a variety of consequences, including death (Brodbelt *et al.*, 2008).

Ketofol is the term coined for the pharmacologically compatible combination of ketamine and propofol (Donnelly *et al.*, 2008). Ketofol CRI (1:2 and 1:1) anaesthesia may be recommended for clinical use for ovariohysterectomy in dogs as they are better anaesthetic combinations clinic-physiologically and haemodynamically (Kalaiselvan, 2018). Doxapram has been used in veterinary medicine in various situations including stimulation of respiration in neonates and arousal from sedation and anaesthesia (Giguere *et al.*, 2007). It has been used for recovery from various sedatives and anaesthetics includingpropofol in dogs (Sabiza *et al.*, 2020).

Recently, potential strategiesare being investigated for fastening the recoveryfrom general anaesthesia as delayed recovery leads to heart, liver, and kidney failure, and all of this can be caused by a compromised respiratory system (Tranquilli *et al.*, 2013). The present study was therefore, undertaken to evaluate the effects of doxapram on recovery parameters and haemato-biochemical variations followingcontinuous rate infusion anaesthesia with ketofol in dogs.

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MATERIALS AND METHODS

The study was conducted on 12 clinical cases of healthy female mongrel dogs, randomly divided in two groups (six animals in each group) which were brought to Departmentof Veterinary Surgery and Radiology, LUVAS, Hisar for elective ovariohysterectomy. The dogs were subjected to physiological and haemato-biochemical examination and kept off feed and water for 12 hours prior to the ovariohysterectomy. Before preparation of animal for surgery atropine sulphate was injected @ 0.04 mg/kg body weight IM, after 5 minutes of that the combination of xylazine @ 2 mg/kg body weight and butorphanol 0.2 mg/kg body weight was injected IM. After 5 minutes of that Meloxicam was injected @ 0.5 mg/kg body weight IM. Immediately after that animal was canulated in the cephalic vein of both forelimbs with the intravenous catheters attached to the normal saline infusion in one limb and with the ketofol infusion pump in another limb. After 10 minutes of xylazine and butorphanol, animals were induced with ketofol I/V (till effect), and immediately after induction, the animals were maintained with theketofol(1:2) CRI @300µg/kg/min. Immediately after completion of the surgery, doxapram (1 mg/kg, I/V) was used in group B while group A was taken as the control group.

Parameters investigated: Recovery parameters–Regain of Pedal reflex and Palpebral reflex, eye-opening time,

Recovery time, Head movement, Sternal recumbency time, Supported walk time, and Non-supported walk time.

Haemato-biochemical parameters - haemoglobin (Hb), total Erythrocytes Count (TEC) and packed cell volume (PCV), total leukocyte count (TLC), differential leukocyte count (DLC), total protein, albumin, glucose, blood urea nitrogen (BUN), creatinine, ALT, AST. Blood and serum sampling was performed preoperatively (T1), just after the stoppage of ketofol CRI (T2), 5 minutes after doxapram administration (T3) and atcomplete recovery (T4).

The statistical analysis was conducted by SPSS v23 software. Pairwise comparison was done using Duncan 't' Test. P-values<0.05 was considered statistically significant.

RESULTS AND DISCUSSION

The Mean ageof dogs was 3.00 ± 1.06 and 3.16 ± 0.79 years and body weight was 17.08 ± 2.48 and 17.50 ± 1.50 Kg in groups A and B, respectively.

Recovery parameters recorded in the present study are presented in table 1. Comparison between the groups revealed that there was significant (p<0.05) lower time taken for the regaining of pedal reflex, palpebral reflex, recovery time, eye-opening time, head movement, sternal recumbency, supported walk time and non-supported walk time in group B. The early recovery from the anaesthetic effect of ketofol may be due to non-selective CNS stimulant property of doxapram as it directly acts at the respiratory centre in the brain stem and causes the carotid and aortic body chemoreceptors stimulation (Zapata and Hofmeister, 2013). Kim *et al.* (2013) also found that after the administration of aminophylline and doxapram drugs, the return to spontaneous breathing, eye-opening and hand squeezing on verbal commands occurred first in the doxapram group.

The results of haemato-biochemical parameters have been presented in table 2. There was non-significant (p>0.05) decrease in Hb,TEC and PCV within the groups at T2, T3 and T4 in comparison to T4 in both the groups. Decline in haemoglobin and PCV values might be due to pooling of circulating red blood cell in spleen or other reservoirs as a secondary effect of reduced sympathetic stimulation (Surbhi *et al.*, 2010). Comparisiom among the group showed non-significant (P>0.05) higher values of Hb and TEC at different time intervals in group A. The mean values of PCV were non-significantly higher at T1 and T2 while significantly higher at T3 and T4 in group A. Similarly, Sabiza *et al.* (2020) reported a non-significant (P>0.05) decrease in RBC, PCV and Hb values following doxapram administration. Hochadel (2015) reported that rapid administration of doxapram resulted in haemolysis.

Table 1. Recovery parameters recorded for different groups (Mean ± SE)

Recovery parameters	Control (A)	Doxapram (B)
Pedal reflex (minutes)	040.33^{b} ± 2.46	010.83^{a} ± 1.22
Palpebral reflex (minutes)	034.67^{b} ± 2.67	008.67^{a} ± 1.26
Recovery time (minutes)	085.33^{b} ± 4.32	044.00^{a} ± 2.42
Eye-opening time (minutes)	046.83^{b} ± 2.41	017.17^{a} ± 1.28
Head movement (minutes)	065.50^{b} ± 3.01	023.00^{a} ± 1.79
Sternal recumbency (minutes)	076.50^{b} ± 4.48	034.67^{a} ± 2.76
Supported walk time (minutes)	090.67^{b} ± 4.52	056.83^{a} ± 3.16
Non-supported walk time (minutes)	126.6^{b} ± 5.42	081.17^{a} ± 3.59

Means bearing different superscripts (a, b) differ significantly (P < 0.05) between treatment groups

Comparison between the groupsrevealed non-significant (P>0.05) difference in TLC at different time intervals. Comparison within the groups revealed a significant (P<0.05) and non-significant (P>0.05) decrease in TLC from time interval T1 to T4 in groupA and B,respectively. The decline in TLC mightbe due to the rise in plasma volume due to vascular pooling after anaesthetic administration or confinement of RBC in the spleen and lungs (Komar *et al.*, 2003). There were non significant changes in mean values of neutrophil, lymphocyte, monocyte, eosinophil and basophil at different time intervalswithin the group as well as among the groups. Sabiza *et al.* (2020) observed significantly lower value of neutrophils after the administration of doxapram in comparison to the baseline value and non significant changes in monocytes, basophils and eosinophilsin the doxapram group in comparison to the saline group.

The total protein and albumin values in both the groups decreased non-significantly (P>0.05) at T2, T3 and T4 in comparison to the T1 time interval. This decrease in total protein in canines may be due to inter-compartmental shifting of fluid, which might have caused haemodilution ultimately leading reduction to in serum protein(Bennet *et al.*, 2009). Comparison between the groups revealed that the total protein value in group B was significantly lower at the T4 time interval. Hochadel (2015) and Sabiza *et al.* (2020) found that the serum albumin and total protein concentrations increased following doxapram administration in dogs. The value of glucose in group A increased non-significantly from T1 to T4time interval. In group B there was a significant (P<0.05) increase in glucose value from T1 to T3 while increased non-significantly from T3 to T4. Sabiza *et al.* (2020) observed a similar increase in glucose value after doxapram administration and at recovery in comparison to the base value in dogs anaesthetized with propofol which may be due to increased level of catecholamine by doxapram.

Table 2. Haemato-biochemical parameters recorded at different time intervals (Mean ± SE)

Parameter	Time point	Control (A)	Doxapram (B)
Hb (g/dl)	T1 (Pre-operative)	15.22 ± 1.46	13.70 ± 1.01
	T2 (After ketofol CRI)	13.18 ± 0.59	12.90 ± 0.57
	T3 (After doxapram)	13.45 ± 0.70	12.60 ± 0.61
	T4 (At recovery)	13.47 ± 0.49	12.58 ± 0.63
TEC (million/mm^3)	T1 (Pre-operative)	7.83 ± 0.53	6.76 ± 0.45
	T2 (After ketofol CRI)	6.82 ± 0.33	6.36 ± 0.27
	T3 (After doxapram)	6.95 ± 0.33	6.23 ± 0.29
	T4 (At recovery)	7.09 ± 0.34	6.26 ± 0.26
PCV (%)	T1 (Pre-operative)	42.95± 1.88	39.32 ± 1.98
	T2 (After ketofol CRI)	39.95± 1.44	37.60 ± 1.12
	T3 (After doxapram)	41.20^{b} ± 0.46	37.00^{a} ± 1.11
	T4 (At recovery)	42.95^{b} ± 1.27	37.27^{a} ± 0.59
TLC (thousands/mm^3)	T1 (Pre-operative)	16.95^{B} ± 1.62	14.72 ± 1.87
	T2 (After ketofol CRI)	14.93^{AB} ± 1.56	14.44 ± 2.12
	T3 (After doxapram)	14.51^{AB} ± 1.43	14.20 ± 2.19
	T4 (At recovery)	13.84^{A} ± 1.46	14.08 ± 2.03
Neutrophil (%)	T1 (Pre-operative)	68.00 ± 1.21	67.66 ± 2.45
	T2 (After ketofol CRI)	69.33 ± 1.14	64.83 ± 3.03
	T3 (After doxapram)	69.00 ± 1.12	65.83 ± 2.12
	T4 (At recovery)	65.66 ± 2.84	62.66 ± 3.87
Lymphocyte (%)	T1 (Pre-operative)	24.33 ± 0.84	24.50 ± 2.59
	T2 (After ketofol CRI)	23.33 ± 1.08	26.33 ± 2.88
	T3 (After doxapram)	23.66 ± 1.30	26.66 ± 2.53
	T4 (At recovery)	26.33 ± 2.41	29.16 ± 3.91
Monocyte (%)	T1 (Pre-operative)	5.50 ± 0.62	5.67 ± 0.33
	T2 (After ketofol CRI)	5.33 ± 0.33	6.33 ± 0.33
	T3 (After doxapram)	5.17 ± 0.31	6.33 ± 0.33
	T4 (At recovery)	6.50 ± 0.72	6.67 ± 0.33
Eosinophil (%)	T1 (Pre-operative)	2.00 ± 0.63	2.00 ± 0.45
	T2 (After ketofol CRI)	1.67 ± 0.56	2.17 ± 0.31
	T3 (After doxapram)	2.17 ± 0.48	1.67 ± 0.33
	T4 (At recovery)	1.33 ± 0.42	1.50 ± 0.34
Basophil (%)	T1 (Pre-operative)	0.17 ± 0.17	0.17 ± 0.17
	T2 (After ketofol CRI)	0.17 ± 0.17	0.33 ± 0.21
	T3 (After doxapram)	0.00 ± 0.00	0.17 ± 0.17
	T4 (At recovery)	0.17 ± 0.17	0.00 ± 0.00
Total Protein (g/dl)	T1 (Pre-operative)	6.75 ± 0.37	5.24 ± 0.36
	T2 (After ketofol CRI)	5.99 ± 0.48	4.95 ± 0.52
	T3 (After doxapram)	6.23 ± 0.47	4.59 ± 0.29
	T4 (At recovery)	6.17^{b} ± 0.36	4.75^{a} ± 0.50
Albumin (g/dl)	T1 (Pre-operative)	2.41 ± 0.11	2.03 ± 0.21
	T2 (After ketofol CRI)	2.20 ± 0.11	1.97 ± 0.23
	T3 (After doxapram)	2.31 ± 0.13	2.01 ± 0.21
	T4 (At recovery)	2.30 ± 0.11	2.03 ± 0.27
Glucose (mg/dl)	T1 (Pre-operative)	111.32 ± 034.62	089.35^{A} ± 031.81

	T2 (After ketofol CRI)	150.03 ± 031.48	$205.65^{B} \pm 031.30$
	T3 (After doxapram)	195.15 ± 042.10	$233.90^{BC} \pm 029.33$
	T4 (At recovery)	203.90 ± 046.48	$244.53^{C} \pm 029.37$
Blood Urea Nitrogen (mg/dl)	T1 (Pre-operative)	17.70 ± 3.09	14.85 ± 1.40
	T2 (After ketofol CRI)	16.05 ± 2.00	14.40 ± 1.43
	T3 (After doxapram)	16.45 ± 2.13	14.65 ± 1.79
	T4 (At recovery)	16.47 ± 1.52	14.28 ± 1.53
Creatinine (mg/dl)	T1 (Pre-operative)	0.24 ± 0.03	0.25 ± 0.05
	T2 (After ketofol CRI)	0.24 ± 0.04	0.24 ± 0.04
	T3 (After doxapram)	0.24 ± 0.03	0.24 ± 0.05
	T4 (At recovery)	0.25 ± 0.04	0.27 ± 0.05
ALT (IU/L)	T1 (Pre-operative)	36.60 ± 06.92	37.20 ± 03.91
	T2 (After ketofol CRI)	32.67 ± 06.68	32.92 ± 05.12
	T3 (After doxapram)	35.20 ± 06.77	37.22 ± 06.25
	T4 (At recovery)	38.32 ± 08.30	36.07 ± 04.50
AST(IU/L)	T1 (Pre-operative)	42.93 ± 07.74	32.90 ± 01.66
	T2 (After ketofol CRI)	33.87 ± 07.91	26.85 ± 04.07
	T3 (After doxapram)	35.32 ± 07.78	26.32 ± 03.11
	T4 (At recovery)	40.63 ± 10.40	26.87 ± 02.94

Means (SE) bearing different superscripts (A, B, C) and(a, b) differ significantly ($P<0.05$) within and between treatment groups, respectively

There was non-significant difference in the BUN, creatinine, ALT and AST values at different time intervals while comparing between and within the groups. Sabiza *et al.* (2020) also found a non-significant difference between saline and doxapram groups for serum urea, creatinine and ALT values at different time intervals whereas significant difference in AST values from control group at recovery. Shinde *et al.* (2018) also observed non-significant BUN and creatinine values in dogs anaesthetized with propofol in group I and with ketofol in group II.

Thus, it was concluded that doxapram can be used for shortening anaesthetic recovery time in dogs anaesthetized with ketofol CRI without appreciable negative impact on haematobiochemical parameters.

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