



Research Article

Hematological Effects of Ketofol in Acepromazine or Medetomidine Sedated Dogs

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ABSTRACT

This was a randomized blinded clinical study conducted to evaluate the effects of ketofol on hematological parameters in acepromazine and medetomidine sedated dogs. Twelve (12) entire male mongrel dogs were randomly divided into two groups (Group A and Group B) of six (6) dogs each. Dogs in Group A were premedicated with acepromazine at 0.1 mg/kg BWT and those in Group B with medetomidine at 0.02 µg/kg BWT. Anaesthesia in both groups was induced and maintained using Ketofol (4.0 mg/kg (2 mg/kg Ketamine and 2 mg/kg Propofol) BWT. This was followed by castration in all dogs and assessment of parameters. Hematological parameters evaluated comprised of total erythrocyte count (TEC), total leucocyte count (TLC), total platelet count (TPC), packed cell volume (PCV) and hemoglobin concentration (Hb). Data was expressed as Mean ±SD and compared between the two groups using student t-test. Statistical significance was set at P<0.05. ACP-Ketofol significantly reduced TEC (P=0.001), TLC (P=0.007), PCV (P=0.02) and Hb (P=0.04) compared to Med-Ketofol. These changes did not lead to any notable deleterious effects in the patients post-operatively and into recovery. However, prudent perioperative monitoring of dogs, more so those under acepromazine-ketofol anaesthesia is imperative so as to reduce anaesthesia related morbidity and mortality.

Key words: Acepromazine, Medetomidine, Ketofol, Hematological effects

INTRODUCTION

Total intravenous anaesthesia (TIVA) is an alternative way for administration of general anaesthetics (Sandham, 2009). In both the veterinary and human field, it seems to be a safer way as it causes less cardiopulmonary depression than inhalation anaesthetics. Furthermore especially in a veterinary field set up, it is more practical as it does not require bulky equipments as inhalant anaesthetics (McKenzi, 2008).

Premedicants (tranquilizers and sedatives) are commonly used in veterinary small animal practice. Among other uses they facilitate handling and as premedicants before general anaesthesia induction (Vesal *et al.*, 2011). Phenothiazines and alpha-2-agonists are often used to reduce anxiety and produce sedation in dogs (Rankin, 2015).

Acepromazine is a phenothiazine derivative and a potent neuroleptic agent with relatively low toxicity (Rankin, 2015). The mode of action of acepromazine is mainly by antagonism of dopamine centrally, resulting in mild to moderate sedation, muscle relaxation and a decrease in spontaneous activity (Vesal *et al.*, 2011).

Acepromazine possesses antispasmodic, hypotensive and hypothermic properties (Lemke, 2007). Acepromazine is reported to cause a decrease in packed cell volume (PCV) and a reduction of platelet aggregation (Rankin, 2015). The PCV reduction (20-30%) in dogs and horses following acepromazine administration was attributed to splenic engorgement after alpha-1-adrenergic receptor blockade (Leise *et al.*, 2007).

Medetomidine is a highly selective alpha-2-adrenoceptor agonist (Rankin, 2015). The onset of sedation, analgesia and muscle relaxation is rapid following intramuscular administration of medetomidine to dogs and cats. When administered to dogs at 30 µg/kg, intramuscularly, significant sedation is evident within 5 minutes and lasts for 1-2 hours (Vainio *et al.*, 1989, Rankin, 2015). Some previous studies have reported a non significant decrease of some hematological parameter following medetomidine administration in dogs. Akbar *et al.*, (2014) reported a decrease in total leucocyte count (TLC) and hemoglobin (Hb). This decrease during the anesthesia period is attributed to shifting of fluid from extravascular to intravascular compartment to maintain normal cardiac output (Wagner *et al.*, 1991; Akbar *et al.*, 2014).

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Ketamine [2-(o-chlorophenol)-2-(methylamino)-cyclohexanone hydrochloride] is a dissociative anaesthetic. It is an anaesthetic that has been in veterinary anaesthesia for decades. Dissociative anaesthetics cause dissociation of the thalamocortical and limbic systems in the CNS (Reich and Silvey, 1989). To minimize the untoward effects of ketamine like catalepsy and muscle rigidity, it is usually used as an adjunct with other drugs. Previous studies where ketamine was used alone and xylazine-ketamine combination, the author reported non-significant decrease in the hemoglobin concentration, packed cell volume, total erythrocyte count, total leukocyte count, lymphocyte, monocyte, eosinophil and basophils. The author attributed the decrease to pooling of circulating blood cells in the spleen and other reservoirs secondary to decreased sympathetic activity (Gebremedhin, 2018).

Propofol, a substituted isopropylphenol (2, 6-diisopropylphenol) is a phenolic compound that is slightly soluble in water. Propofol induces depression by increasing the effects of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA) and decreasing the brain's metabolic activity (Rankin, 2015).

Ketofol is a combination of ketamine and propofol in a predetermined ratio. Injectable anaesthetics, such as propofol or ketamine, offer an alternative option for procedures of short duration or when inhalation anaesthesia may not be possible or practical (White, 1988). The combination of these drugs sought the hemodynamic stability observed when given separately, with the convenience of managing only a single infusion. Furthermore, combining both drugs in a single syringe aims to simplify drug administration (Hui *et al.*, 1995).

In developing countries, including Kenya, the veterinarian acts as both the anaesthetist and surgeon in surgical procedures. There are no trained anaesthesia technicians or veterinary nurses to monitor the patients intra-operatively. There is therefore need for a protocol that is less demanding to the surgeon especially with respect to intraoperative monitoring and yet provides adequate anaesthesia and analgesia for the procedure. A few studies have been reported on TIVA with ketofol in dogs elsewhere in the world. However, the uptake of this technique and protocol in Kenya has been slow. This is due to limited knowledge, skills and experience on the application of the technique. Furthermore, data on the effects of ketofol with either medetomidine or acepromazine as the premedicant on haematological parameters is scant. This study was designed to fill this gap.

MATERIALS AND METHODS

Study location

This entire study was carried out at the University of Nairobi, College of Agriculture and Veterinary Sciences, Upper Kabete campus.

Study design

This was a prospective blinded experimental study in which twelve male dogs were randomly allocated into two groups of six animals each. Dogs in one group were treated using acepromazine + ketofol, while those in the

second group were treated using medetomidine + ketofol. Following treatments, all dogs were castrated and selected hematological parameters were evaluated.

The experimental animals

Twelve (12) male mongrel dogs were used for in this study. The dogs were acquired from willing owners within the vicinity of the Faculty of Veterinary Medicine's Animal Hospital. Once acquired, dogs were subjected to routine clinical examination to screen them for presence of any disease. Only dogs free from clinical disease (s) were recruited into the study. The dogs were housed in individual kennels at the Department of Clinical Studies and fed on commercial dog ration once daily. Water was provided *ad libitum*.

All animals were dewormed using a broad spectrum dewormer (Vermic Total®, Laboratorios Microsules, Uruguay) and ectoparasites controlled using an acaricide (Steladone®, Zagro Singapore PTE Limited) through medical bathing done once a week. The dogs were allowed to acclimatize to their new environment for a period of two weeks before being subjected to the experimental study. During the acclimatization period, dogs were subjected to weekly clinical examination and regular interactions to get them used to handling and manipulation. The twelve dogs were randomly assigned via a computer generated random number table to two treatment groups of six dogs each. The two groups were designated as Group A and B.

Experimental drugs and dosages

The following drugs were used in this study at the specified dosages:

- Acepromazine maleate (0.1mg/kg bodyweight) (Aceprom Inj, Centaur Labs, Isando, South Africa) was administered intramuscularly to sedate the dogs in Group A.
- Medetomidine (0.02mg/kg bodyweight) (Domitor® 1mg/ml, Orion Pharma, Vetoquinol, United Kingdom) was administered intramuscularly to sedate the dogs in Group B.
- Ketofol (4.0 mg/kg bodyweight) was administered intravenously to induce and maintain anaesthesia in all dogs. Ketofol (1:1) was prepared by mixing 2 mg/kg body weight of Ketamine (Ketamine Hydrochloride injection USP, Rotexmedica, Trittau, Germany) and 2 mg/kg bodyweight of Propofol (Propofol® Lipuro 1%, B Braun, India) in the same syringe.

Treatment 1

Each of the six dogs in group A was premedicated using acepromazine (0.1 mg/kg bodyweight) administered intramuscularly and anaesthesia was induced and maintained using ketofol (4.0 mg/kg bodyweight) administered intravenously (Group A or ACP-Ketofol / Acepromazine-Ketofol Group).

Treatment 2

Each of the six dogs in group B was premedicated using medetomidine (0.02 mg/kg bodyweight) administered intramuscularly and anaesthesia was induced and maintained using ketofol (4.0 mg/kg bodyweight)

administered intravenously (Group B or Medetomidine-Ketofol / Med-Ketofol Group).

Experimental procedure

Food and water were withheld from each dog 12 hours before the surgery as a routine pre-anaesthetic preparation. Each dog was weighed before the experiment using a digital weighing scale (Momert® Large Pet Scale, Scandivet). Haematological parameters were assessed before sedation (baseline values). Dogs in Group A were sedated with acepromazine (0.1 mg/kg) while those in Group B were sedated with medetomidine (0.02 mg/kg) administered intramuscularly into the lateral thigh muscle. The anaesthetist was blinded to treatments so as to reduce any bias. Each dog was muzzled and restrained by an assistant during the injections.

Ten minutes after premedication, an intravenous catheter was placed into the cephalic vein of the right forelimb of each dog. The pre-scrotal area for each dog was then shaved, scrubbed and disinfected with 70% ethyl alcohol in preparation for an aseptic surgery while restrained in dorsal recumbency by an assistant on a preparation table. Administration of ketofol intravenously for induction into general anaesthesia was done 30 minutes following sedation. Administration of the ketofol dose was done slowly then dogs were intubated (indicated by loss of the laryngeal reflex during intubation). The pre-calculated induction dose for each dog was administered slowly as a bolus. Following induction and intubation, dogs were moved from the preparation room to the surgical room and positioned on a surgical table in dorsal recumbency with the limbs loosely secured onto the surgical table. A multi-parameter physiological monitor (S. cure, Silverline Meditech Private Limited, S.G. Highway, Ahmedabad, Gujarat, India) was used as an aid for anaesthesia monitoring. The arterial blood pressure was evaluated using Doppler technique using an inflatable cuff around the antibrachium of the non-catheterized forelimb. The cuff was connected to the multi-parameter physiological monitor where the pressure reading was obtained. Dogs were monitored until restoration of the laryngeal reflex (indicated by coughing) was observed following which, top up ketofol at a standardized dose (50% of the induction dose) was administered intravenously as a bolus to all dogs. Orchiectomy (castration) was then performed routinely following an aseptic procedure.

Evaluation of Parameters

Evaluation of haematological parameters

An intravenous catheter was placed into the cephalic vein of each dog and 1 ml of blood at each assessment period collected in vacutainer tubes with Ethylenediaminetetraacetic acid (EDTA) for evaluation of haematological parameters. Blood was collected before sedation (baseline), before induction, 10, 20, 30, 60, 90 and 120 minutes post-induction. The blood samples were evaluated using an automatic cell counter (Celltac MEK-6450K, Nihon Kohden corporation, Tokyo, Japan) for the following; total erythrocyte count (TEC) in millions/mm³, total leucocyte count (TLC) in millions/mm³, total platelet count (TPC) in millions/mm³, packed cell volume (PCV) in % and haemoglobin concentration (HB) in g/dl.

Data was entered into Microsoft Office Excel 2010 and validated and descriptive statistics generated. Parametric data was expressed as means and standard deviation (\pm SD) for comparison between the two treatment groups. Student t-test was applied to determine the statistical difference between the treatments. Statistical significance was set at $P \leq 0.05$.

RESULTS

Total erythrocyte count (TEC)

Mean TEC in animals anaesthetized with ACP-Ketofol declined steadily following sedation and induction of anaesthesia to stand at 4.9 ± 0.9 million/mm³ at 120 minutes post induction. This mean was still lower than the baseline value of 6.6 ± 0.8 million/mm³ (Table 1 and Figure 1).

On the other hand, despite a drop in the mean TEC in animals anaesthetized with Med-Ketofol following sedation and induction of anaesthesia, this trend was short-lived as the lowest value (6.0 ± 1.4 million/mm³) was attained at 10 minutes post-anaesthesia induction, after which the mean TEC started increasing. However, at 120 minutes post-induction the mean TEC (6.5 ± 1.7 million/mm³) was still lower than the baseline value (7.3 ± 1.9 million/mm³) [Table 1 and Figure 1].

Comparison of the effects of the two anaesthesia protocols on TEC (Figure 5) revealed that ACP-Ketofol anaesthesia significantly ($P=0.001$) lowered the TEC compared to the Med-Ketofol anaesthesia protocol.

Total leucocyte count (TLC)

The trend in total leucocyte count in dogs anaesthetized with ACP-Ketofol was a general decline following sedation and induction of anaesthesia, reaching its lowest at 20 minutes post induction (10.8 ± 2.9 10⁶/μL). The TLC was still lower than baseline value (14.3 ± 3.7 10⁶/μL), at the end of the 120 minutes monitoring period (Table 1 and Figure 2). However, these changes were not significant.

The animals anaesthetized with Med-Ketofol experienced the same trend in TLC as those in the ACP-Ketofol group, which declined to reach the lowest at 20 minutes post induction (12.7 ± 5.5 10⁶/μL). The TLC was also still lower than baseline value (14.6 ± 5.1 10⁶/μL), at the end of the 120 minutes monitoring period (Table 1 and Figure 2). However, these changes were not significant.

Overall, animals anaesthetized with ACP-Ketofol attained significantly ($P=0.007$) lower TLC (12.1 ± 1.2 10⁶/μL) when compared to animals in the group anaesthetized with Med-Ketofol (13.8 ± 7.3 10⁶/μL) (Figure 2).

Total platelet count (TPC)

There was a continuous drop in TPC in dogs anaesthetized with ACP-ketofol following sedation and induction of anaesthesia. At the end of the 120 minutes monitoring period, TPC stood at 152.8 ± 140.7 10⁹/μL, a figure still below the baseline value of 300.2 ± 180.7 10⁹/μL. However, these changes were not significant (Table 1 and Figure 3).

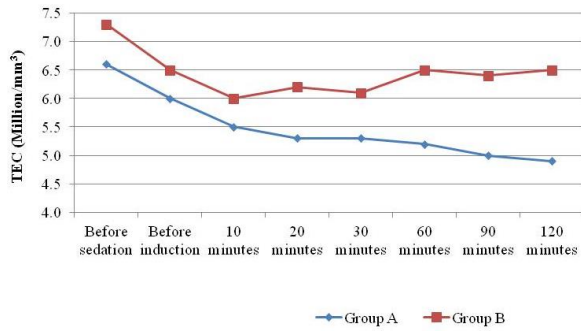


Fig. 1: Trends (mean±sd) in total erythrocyte count (million/mm³) in dogs anaesthetized with ACP-Ketofol (Group A) and Medetomidine-Ketofol (Group B).

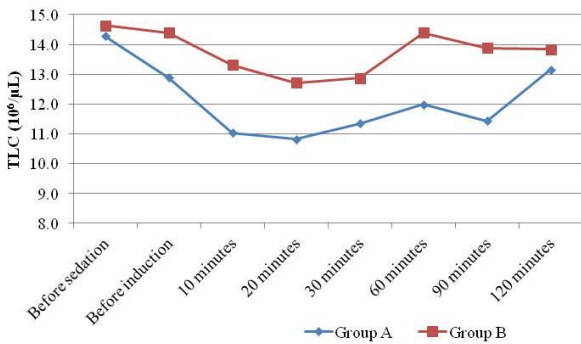


Fig. 2: Trends (mean±sd) in total leucocyte count (10⁶/μL) in dogs anaesthetized with ACP-Ketofol (Group A) and Medetomidine-Ketofol (Group B).

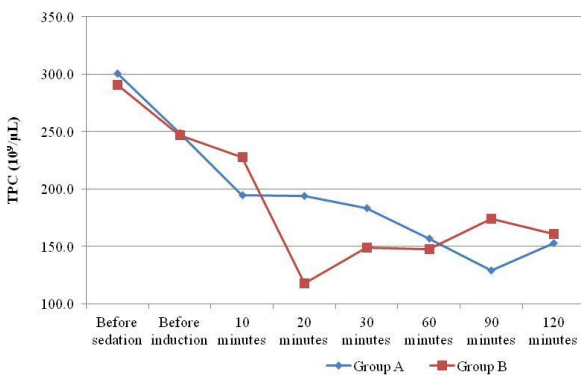


Fig. 3: Trends (mean±sd) in total platelet count (10⁹/μL) in dogs anaesthetized with ACP-Ketofol (Group A) and Medetomidine-Ketofol (Group B).

On the other hand, whereas there was a decline in TPC in animals anaesthetized with Med-Ketofol following sedation and induction of anaesthesia, TPC recorded a minimum value of 117.5±127.4 10⁹/μL at 20 minutes post-induction of anaesthesia. From this point on, TPC started on an upward trajectory. However, at the end of the 120 minutes monitoring period, the TPC value (160.8±199.0 10³/μL) remained below baseline value (290.3±250.210³/μL) However, these changes were not significant (Table 1 and Figure 3).

When the mean TPC values between the two groups were compared, (Figure 3), dogs anaesthetized with ACP-Ketofol had relatively lower TPC values following sedation and anaesthesia as compared to those anaesthetized with Med-Ketofol. However, this difference was not significant (P>0.05).

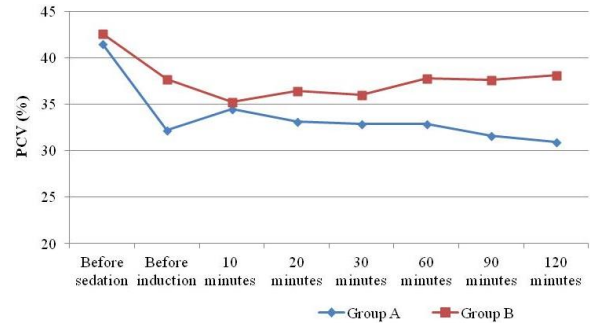


Fig. 4: Trends (mean±sd) in packed cell volume (%) in dogs anaesthetized with ACP-Ketofol (Group A) and Medetomidine-Ketofol (Group B).

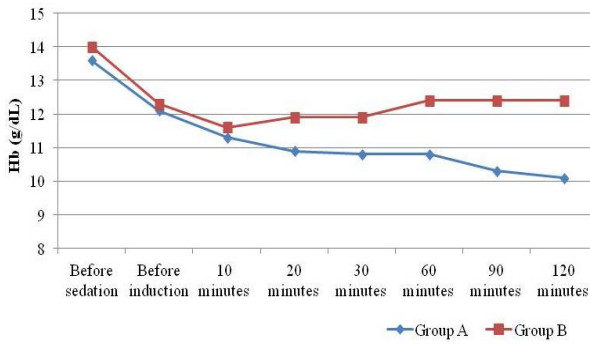


Fig. 5: Trends (mean±sd) in haemoglobin concentration (g/dL) in dogs anaesthetized with ACP-Ketofol (Group A) and Medetomidine-Ketofol (Group B).

Packed cell volume (PCV)

Dogs anaesthetized with ACP-Ketofol had significantly (P<0.05) lower PCV starting 30 minutes after sedation (32.2±6.9 %) compared to the baseline value (41.5±4.2 %). The PCV in this treatment group remained significantly (P<0.05) lower than baseline value up to end of the 120 minutes of monitoring (Table 2 and Figure 4). However, in dogs anaesthetized with Med-Ketofol, PCV decreased from baseline value (42.6±8.4%) following sedation and induction of anaesthesia, recording the lowest value (35.2±7.0%) at 10 minutes following induction of anaesthesia. From this point on, there was a gradual increase in PCV values in this treatment group, but this still remained below baseline value at the end of the 120 minutes monitoring period. However, all these changes were not significant (Table 2 and Figure 4)

When the mean PCV values between the two treatment groups was compared (Figure 4), dogs anaesthetized with ACP-Ketofol had significantly (P=0.02) lower PCV values as compared to dogs anaesthetized with Med-Ketofol.

Haemoglobin concentration (Hb)

Dogs anaesthetized with ACP-Ketofol recorded significantly lower (P≤0.05) Hb concentration starting 10 minutes following induction of anaesthesia, and this maintained the same trend (Table 2 and Figure 5) up to 120 minutes post-induction (10.1±1.3 g/dL) when compared to the baseline value (13.6±1.6 g/dL).

Animals in the other treatment group anaesthetized with Med-Ketofol recorded a general decline in Hb concentration following sedation and induction of

DISCUSSION

anaesthesia. The lowest reading recorded in this treatment group at 10 minutes after induction of anaesthesia was 11.6 ± 2.4 g/dL, compared to the baseline value of 14.0 ± 2.9 g/dL. The mean Hb concentration was still below baseline value at the end of the 120 minutes of monitoring. However, all these changes were not significant (Table 2 and Figure 5).

When the mean Hb concentration values were compared between the two treatment groups (Figure 5), dogs anaesthetized with ACP-Ketofol recorded significantly lower ($P=0.04$) mean Hb concentration compared to dogs anaesthetized with Med-Ketofol.

Table 1: Changes (Mean \pm sd) in Total Erythrocyte Count (TEC), Total Leucocyte Count (TLC) and Total Platelet Count (TPC) in dogs anaesthetized with ACP-Ketofol and Medetomidine-Ketofol

Blood Parameters	Assessment time (in minutes)	ACP-Ketofol group	Med-Ketofol group
Total	Before sedation	6.6 \pm 0.8	7.3 \pm 1.9
Erythrocyte Count (TEC) (million/mm ³)	Before induction	6.0 \pm 2.0	6.5 \pm 1.3
	10	5.5 \pm 1.1	6.0 \pm 1.4
	20	5.3 \pm 1.1	6.2 \pm 1.5
	30	5.3 \pm 1.2	6.1 \pm 1.6
	60	5.2 \pm 1.1	6.5 \pm 1.6
	90	5.0 \pm 0.9	6.4 \pm 1.6
	120	4.9 \pm 1.0	6.5 \pm 1.7
Total Leucocyte Count (TLC) (10 ⁹ / μ L)	Before sedation	14.3 \pm 3.7	14.6 \pm 5.1
	Before induction	12.9 \pm 4.2	14.4 \pm 5.6
	10	11.0 \pm 3.3	13.3 \pm 7.1
	20	10.8 \pm 2.9	12.7 \pm 5.5
	30	11.4 \pm 3.7	12.9 \pm 6.7
	60	12.0 \pm 3.6	14.4 \pm 5.7
	90	11.4 \pm 2.8	13.9 \pm 5.8
	120	13.2 \pm 6.8	13.8 \pm 6.4
Total Platelet Count (TPC) (10 ⁹ / μ L)	Before sedation	300.2 \pm 180.7	290.3 \pm 250.2
	Before induction	248.5 \pm 129.2	247.0 \pm 270.8
	10	194.2 \pm 164.7	227.7 \pm 283.8
	20	193.7 \pm 105.4	117.5 \pm 127.4
	30	183.0 \pm 101.3	148.7 \pm 154.4
	60	157.0 \pm 67.4	147.3 \pm 127.3
	90	128.8 \pm 49.7	173.8 \pm 1428
	120	152.8 \pm 140.7	160.8 \pm 199.0

Table 2: Changes (Mean \pm sd) in Packed Cell Volume (PCV) and Hemoglobin concentration (Hb) in dogs anaesthetized with ACP-Ketofol and Medetomidine-Ketofol

Blood parameters	Assessment time (in minutes)	ACP-Ketofol group	Med-Ketofol group
Packed Cell Volume (PCV) (%)	Before sedation	41.5 \pm 4.2	42.6 \pm 8.4
	Before induction	32.2 \pm 6.9*	37.7 \pm 6.2
	10	34.5 \pm 5.4*	35.2 \pm 7.0
	20	33.1 \pm 4.9*	36.4 \pm 8.1
	30	32.9 \pm 5.4*	36.0 \pm 8.5
	60	32.9 \pm 5.1*	37.8 \pm 8.0
	90	31.6 \pm 4.1*	37.6 \pm 7.8
	120	30.9 \pm 3.8*	38.1 \pm 8.5
Hemoglobin Concentration (Hb) (g/dL)	Before sedation	13.6 \pm 1.6	14.0 \pm 2.9
	Before induction	12.1 \pm 2.8	12.3 \pm 2.1
	10	11.3 \pm 1.6*	11.6 \pm 2.4
	20	10.9 \pm 1.5*	11.9 \pm 2.7
	30	10.8 \pm 1.7*	11.9 \pm 2.9
	60	10.8 \pm 1.6*	12.4 \pm 2.5
	90	10.3 \pm 1.4*	12.4 \pm 2.6
	120	10.1 \pm 1.3*	12.4 \pm 2.7

Key: * - significant ($P<0.05$) difference within group.

Total erythrocyte count (TEC) was reduced in both treatment groups. There aren't lots of reports on haematological effects in dogs anaesthetized with either of the anaesthetic protocols used in this study. It has been postulated that the reduction in TEC could be explained by the alpha-adrenergic blocking effect of acepromazine which might cause relaxation of the spleen consequently leading to splenic sequestration of erythrocytes (Jain, 1993; Gebremedhin, 2018). In other species as well, haematological parameters including TEC, packed cell volume (PCV) and haemoglobin concentration (Hb) were lower in blood samples collected from skunks anaesthetized with the combination of acepromazine / ketamine (Crooks *et al.*, 2003). A different study where subjects were administered the drug combinations xylazine-ketamine / acepromazine -propofol / acepromazine -butorphanol-metacam-propofol reported that the total erythrocyte counts as well as haemoglobin content and haematocrit of cats under all three anesthetic protocols were significantly reduced immediately after drug administration and before the surgery (Zlateva and Marino, 2015). The authors also suggested that changes in those parameters were due to direct effects of the anaesthetic drugs on organs causing vasodilation of smooth vascular muscles and hormone mediated effects (suppression of catecholamine release) (Wilson *et al.*, 2004). Previous studies in cats demonstrated that the intravenous or intramuscular administration of ketamine resulted in substantial repeated decline in haematocrit values and red blood cell counts (Frankel and Hawkey, 1980; Pfeil and Dueterberg, 1987). Contrary to that, the subcutaneous injection, which is not the usual route of administration, caused an increase in haematocrit values (Regnier and Guelfi, 1982). It is established that ketamine acts directly towards smooth muscle vasodilation. Apart from ketamine, propofol and acepromazine also cause vasodilation thus altering the vascular wall tone (Wilson *et al.*, 2004). These effects of anaesthetics explain the vasodilation of splenic blood vessels, occasioning the changes in haematological parameters during anaesthesia (Altura *et al.*, 1980, Tweed *et al.*, 1972; Leise *et al.*, 2007; Gebremedhin 2018). Therefore, it is not recommended to administer acepromazine in cases with blood loss (Crooks *et al.*, 2003). Furthermore, since both protocols resulted in a reduced TEC, hypovolemic surgical patients will require extra care and monitoring throughout the pre, intra and post surgical period. This is especially when acepromazine -ketofol is the protocol in use as it was found to significantly reduce TEC among treatment subjects.

Both treatment groups experienced a relative decline in mean total leucocyte count (TPC). However, there was a significant difference in mean TLC between the two protocols. The drop in mean TLC is consistent with findings from a study in White-Tailed Deer anaesthetized with acepromazine -ketamine (Ahmed *et al.*, 2009). The authors suggested that the significant decline in TLC 20 minutes after acepromazine administration and 30 minutes after ketamine would be explained by the alpha-adrenergic blocking effect of acepromazine inducing relaxation of the spleen and consequently causing splenic

sequestration (Jain, 1993). Similarly, administration of alpha-2-agonists has been shown to suppress the circulating catecholamines therefore exerting a modulating effect on leukocyte subpopulations. Dissociative agents (e.g. Ketamine) also reduce leukocyte counts (Umar and Adam, 2013).

A significant drop in packed cell volume (PCV) was noted among subjects anaesthetized with acepromazine - ketofol while dogs that were anaesthetized with medetomidine -ketofol only experienced a slight drop. The effect of acepromazine on PCV in dogs in the current study is consistent with previous studies where authors suggested that PCV decreases by 20-30% within 30 minutes of acepromazine administration in dogs and horses. Furthermore, the PCV remains well below baseline values for at least 120 minutes as was the case in this study (Lang *et al.*, 1979; Ballard *et al.*, 1982; Marroum *et al.*, 1994; Leise *et al.*, 2007). The mean haemoglobin concentration (Hb) was significantly low among dogs that were anaesthetized with acepromazine - ketofol while Hb among subjects that were anaesthetized with medetomidine -ketofol remained fairly stable. It is reported from studies carried out in white-tailed deer that, Hb and PCV slightly decreased 20 minutes after the administration of acepromazine and 30 minutes after the administration of ketamine. This can be explained by the alpha-adrenergic blocking effect of acepromazine which might induce relaxation of the spleen and consequently cause splenic sequestration of erythrocytes (Jain, 1993). In horses, studies have shown that PCV decreased over time after the administration of acepromazine (Marroum *et al.*, 1994). Previous studies have suggested that pooling of circulating blood cells in the spleen and other reservoirs secondary to decreased sympathetic activity could be the reason for a decrease in Hb, PCV, and TLC (Pawde *et al.*, 2000; Kilic, 2004;). Furthermore, the decrease in PCV and Hb during the period of anaesthesia or sedation might be attributed to the shifting of fluid from extravascular compartment to intravascular compartment in order to maintain normal cardiac output in the animals (Wagner *et al.*, 1991).

Conclusions

ACP-ketofol protocol significantly reduced most hematological parameters. However, these changes did not lead to any notable deleterious effects in the patients post-operatively and into recovery. Prudent perioperative monitoring of dogs, more so those under acepromazine-ketofol anaesthesia is imperative so as to reduce anaesthesia related morbidity and mortality.

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