

Evaluation of Physical and Haemato-Biochemical Parameters after Administration of Different Doses of Propofol in Xylazine-Ketamine Premedicated Dogs

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Abstract

The present study was designed to investigate the changes of physical and haemato-biochemical parameters after administration of three different doses of propofol in dogs premedicated with xylazine and ketamine. The study was carried out on five clinically healthy male mongrel dogs. They were subjected to three treatments, with 2 weeks apart. The animals in the three groups were premedicated with intravenous injection of 0.5 mg/kg of xylazine HCL and 2 mg/kg of ketamine HCL. 4, 6 and 8 mg/kg of propofol were administered 15 minutes after xylazine-ketamine combination in the 1st, 2nd, and 3rd groups respectively. The different physical, hematological and biochemical parameters were evaluated before, during and after anesthesia of animals. The results revealed that there was no significant difference between the three doses of propofol in the onset, duration and recovery of anesthesia. There were significant decreases ($P < 0.05$) of respiratory rate in group I and III. The body temperature significantly decreased in the 1st treatment. The incidence of apnea increased with the uses of 6 and 8 mg/kg of propofol. Regarding the hematological values, there were significant decreases of hemoglobin concentration and mean corpuscular hemoglobin concentration (MCHC) during and after recovery of anesthesia in the 1st group. The biochemical parameters did not show clear changes in all groups, except GGT in the 1st group which increased significantly after recovery of anesthesia ($P < 0.05$). In the lipid profile, the cholesterol and low-density lipoprotein (LDL) showed significant decreases ($P < 0.05$). According to the obtained results, it could be concluded that the use of different doses of propofol has a little effect on different physical, hematological and biochemical parameters. These changes may appear in animals received the propofol for the first time. The uses of different doses of propofol mostly result in the same anesthetic effect regarding the onset, duration, and recovery. The increase of propofol dose may be associated with some adverse effects such as the respiratory depression and apnea. It is recommended that the use of a dose of 4 mg/kg of propofol in premedicated animals provided that the injection of propofol should be carried out slowly.

Keywords: Biochemical Parameters; Dogs; Hematological; Physical Signs; Propofol; Xylazine-Ketamine

Abbreviations

EDTA: Ethylene Diamine Tetra Acetic Acid; TRBCs: Red Blood Cells; TWBCs: Total White Blood Cells; PCV: Packed Cell Volume; MCV: Mean Corpuscular Volume; MCH: Mean Corpuscular Hemoglobin; MCHC: Mean Corpuscular Hemoglobin Concentration; ALP: Alkaline Phosphatase; GGT: Gamma Glutamyl Transferase; AST: Aspartate Aminotransferase; ALT: Alanine Aminotransferase; HDL: Total Cholesterol, High Density Lipoprotein; LDL: Low Density Lipoprotein; VLDL: Very Low-Density Lipoprotein; SD: Standard Deviation; ANOVA: Analysis of Variance; LSD: Least Significant Difference

Introduction

Propofol is a unique non-barbiturate, non-steroid, short-acting general intravenous anesthetic agent [1]. It is belonging to the alkyl phenol group. It has a rapid onset of action, poor analgesic effect, good muscle relaxation properties, and is associated with a complete and excitement-free recovery from anesthesia [2]. It is the most widely used hypnotic agent for induction of anesthesia [3]. Nowadays in human and animal practice, it is used for sedation, induction of anesthesia, and maintenance of anesthesia when administered as a constant rate infusion (CRI) [4]. In the literatures, propofol has the several advantages and disadvantages. Because of its short duration of action after a single injection, it may not be considered as an anesthetic of choice for procedures requiring prolonged anesthesia. However, if propofol is the preferred induction agent for different surgical procedures, it is essential that anesthesia can be maintained by continuous intravenous infusion or intermittent bolus injections of propofol [5-7], or other intravenous agents [8,9]. The addition of other drugs with propofol may aim to the reduction of the side effects and improvement of anesthetic quality. Xylazine HCL is α 2- adrenoceptor agonist that widely used in small animal practice [10,11]. It is considered a common agent of the drugs which are used for premedication in some countries. This may be due to its availability relative to other drug members, its low price, and its outstanding sedative and analgesic effects [10,12]. The use of ketamine HCL for sedation/restraint in the pre-anesthetic period was reported in the literatures [13]. The authors [13] added that the ketamine when will be used as a pre-anesthetic, should not be administered as a sole agent, but other agents should be added such as acepromazine, α -2 agonists, or benzodiazepines. These combinations of drugs are commonly used in cats other than dogs.

The aim of the present study was to investigate the effect of different doses of propofol in dogs premedicated with xylazine-ketamine. The onset, duration, recovery, physical parameters, hematological and biochemical findings were evaluated.

Materials and Methods

Animals

Five clinically healthy adult mongrel dogs were selected for this study. They were male; and their ages and weight ranged from 1 - 2 years and 12 - 16 kg respectively. The dogs were subjected to three treatments. Two weeks interval passed between different treatments.

The study protocol was approved by the institutional ethics committee of the faculty of veterinary medicine, Assiut University, Egypt. The animals were enclosed in well-equipped room in animal hospital, Assiut University. The food and water were provided to animals in a continuous manner. The dogs were dewormed using praziquantel (5 mg/kg p.o.- EIPICO company, Egypt) and Ivomac (Ivermectin; 0.2 mg/kg/week for 4 weeks- Merial company, Boehringer Ingelheim Vetmedica). They accommodated the place and individuals.

The dogs were subjected to physical examination. The temperature, heart rate and respiratory rate were recorded and tabulated before administration of anesthetic agents. The hydration status and the capillary refilling time were evaluated. The mental status of the dogs was examined. The consciousness (normal or depressed) and behavior (normal, calm or aggressive) were considered. The commonly examined cranial nerves (CN II, V and VII) were checked for integrity. The pupillary light, palpebral, corneal reflexes, menace response and jaw tone were evaluated. The posture and gait of dogs were inspected. The postural reactions were carried out to detect any neurological deficits which could not be detected during the stance and walking of the animals. The withdrawal reflex in the front and hind limbs, and the patellar reflex in the hind limbs were selected for examination.

Anesthetic protocol

The dogs were subjected to 3 anesthetic treatments with 2 weeks interval between them. The dogs received in each regime the same dose of xylazine HCL and ketamine HCL, but different dose of propofol. The different anesthetic protocols were carried out as the followings:

- **First group:** I.V combination of 2 mg/kg.b.w of ketamine (Ketamine Rotexmedica 50 mg/ml, Arzneimittelwerk GmbH Rotexmedica, Germany), and xylazine (0.5 mg/kg.b.w; XYLA-JECT 2%, Adwia Pharmaceuticals Co. 10th of Ramadan city, Egypt) then 15 minutes interval followed by IV injection 4 mg/kg.b.w of propofol (deprivan 10 mg/kg (1%) - corden pharma SpA, Caponago, Italy).
- **Second group:** I.V combination of ketamine (2 mg/kg.b.w), and xylazine (0.5 mg/kg.b.w) then 15 minutes interval followed by IV injection of propofol (6 mg/kg.b.w).
- **Third group:** I.V combination of ketamine (2 mg/kg.b.w), and xylazine (0.5 mg/kg.b.w) then 15 minutes interval followed by IV injection of propofol (8 mg/kg.b.w).

The physical parameters were recorded after administration of xylazine-ketamine drugs. As well as they were recorded after 10, 20, 30 and 40 minutes passed from propofol injection, and after recovery from anesthesia. The onset, duration and other signs were recorded after propofol administration.

Blood samples

9 ml of blood was obtained from the jugular vein and divided into plain, EDTA and heparinized tubes. The blood in the latest tubes was thoroughly agitated to mix well with anti-coagulants. The tubes were kept for hematological and biochemical analysis.

Hematological analysis

Whole blood samples were collected in vacutainer tubes containing EDTA (Ethylene Diamine Tetra Acetic acid) as anticoagulant and were subjected to hematological analysis according to Coles., *et al.* (1986) [14]. Red blood cells (TRBCs) count and total white blood cells (TWBCs) count were measured using hemocytometer method. Differential leucocytes count was performed by using a stained blood film. Hemoglobin concentration was measured by using commercial test kits supplied by spectrum diagnostics (Spectrum Diagnostics, Cairo, Egypt) and means of Digital VIS/Ultraviolet Spectrophotometer (Optizen 3220 UV, Mecasys Co. Ltd, Korea). Packed cell volume (PCV %) was measured using microhematocrit method. Mean corpuscular volume (MCV, fl), mean corpuscular hemoglobin (MCH, pg) and mean corpuscular hemoglobin concentration (MCHC, g/dl) were calculated mathematically.

Biochemical analysis

Blood samples for separation of serum were collected in plain vacutainer tube and processed for separation of serum according to Coles., *et al.* (1986) [14]. Serum samples were used for measuring serum total proteins, albumin, globulins, blood urea, creatinine, alkaline phosphatase (ALP), gamma glutamyl transferase (GGT), aspartate aminotransferase (AST), alanine aminotransferase (ALT), total cholesterol, high density lipoprotein (HDL), low density lipoprotein (LDL), very low density lipoprotein (VLDL) and triglycerides. The heparinized blood sample was used for measurement of plasma lactate level. All parameters were measured using commercial test kits supplied by Spectrum Diagnostics (Egyptian company for biotechnology, Cairo, Egypt) and by means of Digital VIS/Ultraviolet Spectrophotometer (Optizen 3220 UV, Mecasys Co. Ltd, Korea).

Statistical analysis

Data were presented as mean and standard deviation (mean \pm SD). The data were analyzed using statistical package for the Social Sciences for Windows (SPSS, version 21, Chicago, IL, USA). Repeated measure ANOVA was used for comparison of the physical parameters post-injection of drugs to the pre-treatment values (time zero). One way ANOVA was used for comparison of the means of onset and duration of the different groups. Data of the hematological and biochemical parameters after injection at different times were comparing

with those at the pre-injection using one-way ANOVA and tested for differences using Post-hoc test, Least Significant Difference (LSD). Statistically significant differences were determined at $p \leq 0.05$.

Results

Physical parameters

Group 1

It was recorded non-significant changes in body temperature along the time after anesthesia relative to the basal value, but there a significant decrease of body temperature at 40 minutes relative to the body temperature at 20 minutes after injection of propofol. There were significant changes in heart rate along the time of anesthesia. There was a significant decrease in heart rate after xylazine-ketamine administration relative to the basal heart rate, and then it increased significantly after 10 minutes of propofol administration. Also, the respiratory rate showed a significant variation. There was a significant decrease in respiratory rate after xylazine-ketamine administration then gradually increased after propofol administration but non-significantly. All the physical data were expressed in table 1.

Group 2

The physical parameters (temperature, heart rate and respiratory rate) did not show any significant changes either after xylazine-ketamine or propofol administration relative to the values before anaesthetic. Table 1 exhibited these results.

Group 3

The temperature and heart rate in the third group which received 8 mg/kg of propofol did not change substantially. Concerning to, the respiratory rate there was a significant variation. It showed significant decrease after xylazine-ketamine administration which continued till 10 minutes passed after propofol administration then significant increases were recorded till recovery. Table 1 summarized the data.

Time	Group I			Group II			Group III		
	RR	HR	T	RR	HR	T	RR	HR	T
Before	15.25 ± 2.5 ^{a,b,c}	78 ± 14.67 ^a	38.95 ± .8	16.5 ± 1	63.75 ± 14.36	38.53 ± 0.71	25.5 ± 6.2 ^{a,b}	55.5 ± 3.2	38.7 ± 0.34
X-K	10.75 ± 0.96 ^a	54 ± 4.9 ^{a,b,c}	38.98 ± .6	14.50 ± 3	60 ± 4.24	38.8 ± 0.24	18.5 ± 6.81 ^a	55.5 ± 6.2	38.9 ± 0.4
Pro 10	13 ± 3.8	71.25 ± 9.9 ^b	38.3 ± 1.1	15.25 ± 1.5	65.25 ± 11.59	38.7 ± 0.99	12 ± 2.83 ^{b,c}	56 ± 3.92	38.8500 ± .54467
Pro 20	13.25 ± 4.3	69 ± 11.489	38.15 ± 0.87 ^a	15 ± 2	68.25 ± 8.96	38.6 ± 1.02	18. ± 5.4	54 ± 4.97	38.5000 ± .77028
Pro 30	10.5 ± 1.9 ^b	66.75 ± 6.18 ^c	37.95 ± .98	16 ± 2.31	63.75 ± 6.2	38.43 ± 1.26			
Pro 40	11.25 ± 0.96 ^c	66.75 ± 6.18	37.83 ± 0.95 ^a	15 ± 2	63.75 ± 6.65	38.38 ± 1.18			
Recovery	12.2500 ± 4.3	72.75 ± 13.05	37.93 ± 1.1	16.5 ± 3.4	77.25 ± 15.17	38.2 ± 1.17	20 ± 2.83 ^c	52.5 ± 3.8	38.45 ± 0.6

Table 1: The respiratory rate, heart rate and temperature before and after injection of anesthetic agents in the three different groups (Group I= 4mg/kg of propofol, Group II= 6 mg/kg of propofol, Group III= 8 mg/kg of propofol).

Legend: RR= Respiratory rate, HR= Heart rate, T= Temperature, X-K= xylazine-ketamine, pro 10= 10 minutes after injection of propofol, pro 20= 20 minutes after injection of propofol, pro 30= 30 minutes after injection of propofol, pro 40= minutes after injection of propofol
There were significant differences between the values which were superscripted by same letter.

Duration and onset

There were no significant changes between the three groups either in the onset, duration and different reflexes. It was noticed that two dogs in the first group suffered vomiting after injection of xylazine administration. In the other two groups, no animal had vomiting. The apnea (stop of respiration) was recorded in all animals in the group 2 and 3, while just two animals suffered apnea in group one.

Hematological picture

According to the blood picture, there was a significant decrease in hemoglobin concentration and MCHC ($P < 0.05$) after recovery from anesthesia post-administration of 0.5ml/kg b.w of xylazine, 2 ml/kg b.w. of ketamine and 4 ml/kg.bw. of propofol table 2.

Group	RBCs count (x10 ⁶)	Hb. Conc. (g/dl)	PCV (%)	MCV (fl)	MCH (pg)	MCHC (%)	T. WBCs count (x10 ³)/mm ³	Neutrophils Count (x10 ³)/mm ³	Band cell Count (x10 ³)/mm ³	Lymphocytes Count (x10 ³)/mm ³	Eosinophils Count (x10 ³)/mm ³	Monocytes Count (x10 ³)/mm ³
A1	8.10 ± 2.31a	15.64 ± 1.34a	41.00 ± 2.58a	52.79 ± 10.40a	20.48 ± 5.76a	38.35 ± 5.01a	15.26 ± 5.65a	11.89 ± 5.46a	0.18 ± .20a	1.51 ± 2.13a	0.19 ± 0.12a	1.48 ± .97a
A2	6.15 ± 2.62a	13.13 ± 0.94b	40.00 ± 3.82a	72.68 ± 26.12a	24.69 ± 11.32a	33.17 ± 5.08b	12.23 ± 6.07a	8.69 ± 3.03a	0.00 ± 0.00a	1.84 ± 2.63a	0.45 ± 0.16a	1.24 ± .68a
A3	7.26 ± 2.78a	12.60 ± 1.55b	40.75 ± 4.19a	60.85 ± 17.24a	18.73 ± 4.99a	30.99 ± 2.74b	14.18 ± 8.80a	10.02 ± 6.48a	0.15 ± .10a	2.14 ± 2.30a	0.00 ± 0.00a	1.8 ± 1.53a
B1	5.96 ± 1.09a	14.34 ± 2.30a	42.50 ± 6.95a	71.61 ± 4.07a	24.17 ± 1.35a	33.76 ± 0.37a	10.76 ± 2.78a	5.84 ± 1.37a	0.00 ± 0.00a	2.57 ± 1.91a	.74 ± 1.04a	1.60 ± 0.63a
B2	6.07 ± 1.64a	12.62 ± 1.88a	39.00 ± 6.58a	66.75 ± 15.52a	21.50 ± 4.18a	32.44 ± 1.42a	10.81 ± 2.80a	5.68 ± 2.84a	0.06 ± 0.02a	2.84 ± 2.20a	.99 ± 1.11a	1.21 ± 0.63a
B3	5.15 ± .13a	12.89 ± 1.12a	39.33 ± 4.93a	76.47 ± 11.64a	25.05 ± 2.83a	32.88 ± 1.29a	11.20 ± 3.96a	6.57 ± 2.27a	0.41 ± 0.06a	2.65 ± 2.47a	.82 ± 1.103a	0.72 ± 0.34a
C1	6.49 ± 1.33a	13.67 ± 1.21a	41.50 ± 3.10a	65.43 ± 10.78a	21.49 ± 3.01a	32.94 ± 1.04a	13.52 ± 1.66a	6.84 ± 1.51a	0.00 ± 0.00a	3.10 ± 1.84a	1.91 ± 1.78a	1.65 ± 1.43a
C2	5.97 ± .97a	12.37 ± .88a	37.75 ± 4.27a	63.96 ± 8.84a	21.01 ± 2.86a	32.89 ± 1.60a	11.57 ± 3.60a	6.49 ± 1.16a	0.07 ± 0.05a	2.60 ± 2.01a	1.11 ± 1.73a	1.29 ± 1.22a
C3	6.23 ± 1.20a	12.19 ± 2.17a	37.00 ± 4.96a	60.43 ± 9.13a	19.81 ± 3.04a	32.85 ± 2.54a	12.51 ± 3.20a	6.79 ± .84a	0.26 ± 0.16a	3.26 ± 2.86a	1.28 ± 1.34a	0.91 ± 0.75a

Table 2: Haematological parameters in the three different groups before, during and after recovery from anesthesia.

There were significant differences ($p < 0.05$) between values with different letters in the same group (A= group I, B= group II, and C= group III; 1,2 and 3 represented before, during and after recovery from anesthesia).

Regarding to the groups 2 and 3, there were no significant changes in all measured blood constituents as shown in table 2.

Biochemical parameters

In serum biochemical constituents, there was a significant increase ($P < 0.05$) in serum GGT activity after recovery from administration of 0.5ml/kg b.w of xylazine, 2 ml/kg b.w. of ketamine and 4 ml/kg.bw. of propofol as expressed in table 3. The lipid profile showed a

significant decrease in serum total cholesterol and LDL level ($P < 0.05$) after recovery from administration of 0.5ml/kg b.w of xylazine, 2 ml/kg b.w. of ketamine and 4 ml/kg.bw. of propofol as was exhibited in table 4.

Group	Total protein (g/dl)	Albumin (g/dl)	Globulins (g/dl)	A/G ratio	Creatinine (mg/dl)	Urea (mg/dl)	Lactate (mg/dl)	ALT (U/l)	AST (U/l)	GGT (U/l)
A1	4.85 ± 0.78a	2.18 ± 0.38a	2.67 ± 0.73a	0.86 ± 0.26a	1.05 ± 0.42a	39.85 ± 18.05a	37.87 ± 19.98a	69.10 ± 29.31a	115.57 ± 52.83a	3.97 ± .83a
A2	4.49 ± 0.36a	2.03 ± 0.47a	2.45 ± 0.46a	0.87 ± 0.33a	1.14 ± 0.29a	41.41 ± 22.78a	26.45 ± 19.35a	77.29 ± 31.30a	108.37 ± 41.30a	3.64 ± 1.32a
A3	4.53 ± 0.67a	2.02 ± 0.45a	2.51 ± 0.80a	0.89 ± 0.39a	1.22 ± 0.32a	37.67 ± 16.92a	17.60 ± 6.44a	82.69 ± 32.16a	58.34 ± 33.24a	6.92 ± 1.52b
B1	5.69 ± 1.26a	2.86 ± 0.81a	2.82 ± 0.51a	1.01 ± 0.19a	0.96 ± 0.30a	32.02 ± 10.94a	11.32 ± 5.66a	186.54 ± 40.65a	162.65 ± 87.84a	3.16 ± 2.21a
B2	4.66 ± 0.31a	2.68 ± 0.70a	1.97 ± 0.83a	1.73 ± 1.25a	0.95 ± 0.22a	35.51 ± 9.81a	8.03 ± 4.01a	226.21 ± 41.63a	159.66 ± 61.63a	5.91 ± 3.63a
B3	5.20 ± 0.50a	2.82 ± 0.42a	2.37 ± 0.71a	1.41 ± .80a	1.09 ± 0.13a	30.80 ± 10.52a	4.01 ± 2.31a	173.93 ± 27.66a	124.41 ± 68.94a	2.73 ± 1.44a
C1	4.64 ± 0.23a	2.29 ± 0.27a	2.34 ± 0.36a	1.01 ± 0.27a	1.62 ± 0.31a	47.15 ± 20.05a	31.42 ± 4.53a	31.13 ± 21.84a	24.15 ± 3.05a	18.33 ± 1.78a
C2	4.77 ± 0.79a	2.18 ± 0.24a	2.59 ± 0.64a	0.86 ± 0.16a	1.50 ± 0.17a	41.50 ± 16.85a	25.40 ± 4.84a	16.87 ± 7.26a	29.68 ± 20.34a	15.69 ± 3.10a
C3	4.84 ± 0.78a	2.21 ± 0.28a	2.63 ± 0.93a	0.95 ± 0.47a	1.49 ± 0.41a	42.41 ± 21.00a	26.15 ± 6.56a	24.44 ± 14.38a	25.89 ± 18.36a	18.80 ± 1.98a

Table 3: Different biochemical parameters in the three different groups before, during and after recovery from anesthesia. There were significant differences ($p < 0.05$) between values with different letters in the same group (A= group I, B= group II, and C= group III; 1,2 and 3 represented before, during and after recovery from anesthesia).

Group	Triglycerides (mg/dl)	Cholesterol (mg/dl)	HDL (mg/dl)	LDL (mg/dl)	VLDL (mg/dl)
A1	128.81 ± 45.09a	300.46 ± 48.89a	130.34 ± 36.54a	144.32 ± 45.13a	25.76 ± 9.01a
A2	156.47 ± 90.14a	228.76 ± 28.48ab	117.94 ± 33.66a	79.52 ± 13.39b	31.29 ± 18.02a
A3	100.02 ± 15.03a	211.84 ± 56.26b	137.77 ± 35.24a	56.68 ± 26.48b	17.38 ± 6.04a
B1	183.93 ± 79.05a	232.19 ± 40.48a	99.59 ± 60.69a	95.84 ± 55.41a	36.78 ± 15.80a
B2	196.83 ± 67.91a	214.40 ± 41.33a	50.49 ± 30.21a	124.54 ± 50.95a	39.36 ± 13.58a
B3	155.80 ± 70.02a	211.52 ± 44.87a	85.04 ± 33.95a	95.32 ± 41.02a	31.15 ± 14.00a
C1	182.74 ± 59.94	230.15 ± 26.64a	123.29 ± 24.04a	70.30 ± 21.89a	11.98 ± 5.99a
C2	199.41 ± 88.86a	226.65 ± 46.36a	95.72 ± 22.60a	91.04 ± 49.40a	17.77 ± 8.88a
C3	190.29 ± 74.83a	224.32 ± 34.40a	105.95 ± 35.29a	80.30 ± 15.59a	14.96 ± 7.48a

Table 4: Lipid profile in the three different groups before, during and after recovery of anesthesia. There were significant differences ($p < 0.05$) between values with different letters in the same group (A= group I, B= group II, and C= group III; 1, 2 and 3 represented before, during and after recovery from anesthesia).

Discussion

The goal of the present study was to investigate and compare the effect of different doses of propofol in dogs which were premedicated by xylazine-ketamine. The onset, duration, recovery, different reflexes, the physical parameters, the hematological and biochemical parameters were evaluated. The results of this study revealed that the use of 4mg/kg of propofol in xylazine-ketamine pre-medicated dogs gave satisfactory results with low side effects relative to other two different doses.

The results of the present study revealed that the use of 4mg/ kg b.w of propofol leads to significant decrease of body temperature. This result is consistent with the results of previous studies [15,16]. This may be attributed to the physiological effects of the anesthetic agents and reduction in muscle activity of anesthetized animals [15]. As well as the recumbent position of unconscious animals during anesthesia and the environmental temperature around anesthetized animals may be incriminated in reduction of body temperature [17,18]. However, the use of other doses (6 and 8 mg/kg b.w of propofol) did not cause any significant difference in body temperature.

The present work revealed that 0.5mg/kg b.w of xylazine, 2 mg/kg b.w. of ketamine and 4mg/ kg b.w of propofol lead to significant variation in heart rate. There was a significant decrease in heart rate (HR) after xylazine-ketamine administration [2,16,19]. Thus, the presence of the cardiac stimulant as ketamine may not have the substantial effect on the heart to mask or overcome the bradycardia effect of xylazine HCL [16]. This decrease of HR was followed with a significant increase but after 10 minutes of propofol administration which was in accordance with the results reported in sheep and horse [20,21]. Then a non-significant decrease in heart rate 30 minutes after propofol administration was recorded. A transient severe bradycardia following propofol induction has been reported in the pregnant ewe [22]. and dogs [23]. This fluctuation of HR may be ascribed to the changes of plasma concentration of propofol. It gives a high effect shortly after administration then its concentration gradually decreases due to rapid hepatic biotransformation and renal excretion [16]. However, 6 and 8 mg/kg b.w of propofol did not cause any significant difference in heart rate. This non-significant effect of the latter doses could not be fully elucidated.

In the present study, it was found that 4 and 8 mg/ kg b.w of propofol lead to significant decrease of respiration. These results were in accordance with the results of previous work which carried out in sheep and horse [20,21]. The decrease of respiratory rate is occurred due to a central effect. Although the respiratory depression may result in accumulation of carbon dioxide (hypercapnia) and then respiratory acidosis, the anesthetized dogs showed decrease of respiration and some suffered apnea [24]. The used dose 6 mg/kg b.w of propofol did not cause any significant difference in respiratory rate.

The significant decreases of hemoglobin concentration, MCHC, PCV and total erythrocyte count (TEC) after administration of 4 mg/ kg of propofol in the present study were in agreement with has been reported in the previous studies [25-28]. These changes may be due to sequestration of red blood cells in nonsplenic sites. This hypothesis was verified in the previous studies in dogs. They demonstrated that propofol does not cause measurable splenic enlargement [29,30]. Additionally, Wilson., *et al.* (2004) [30], described a lack of correlation between hematocrit and spleen size following the anesthetic protocols with acepromazine and propofol suggesting sequestration of red blood cells in nonsplenic sites and the decrease in blood cell count due to the drugs commonly used in anesthesia practice could significantly affect the oxidant-antioxidant environment of immune cells such as peripheral blood lymphocytes. In contrast to the present findings, Soordaya., *et al.* (2001) [31] reported an increase in Hb on induction with propofol in dogs. However, 6 and 8 mg/kg b.w of propofol did not cause any significant difference in red blood cells (He), hematocrit (Ht), hemoglobin concentration (Hb) and total leukocyte count (Le) as basophils, eosinophils, band neutrophils, segmented neutrophils, monocytes, lymphocytes and platelets. These results were consistent with the reported results by Garcia-Navarro and Pachaly., *et al.* (1994) [32]. In the present study, the values of total leukocyte counts, platelets, differential leukocyte counts (neutrophil, eosinophil, lymphocyte and monocyte) recorded at different intervals showed non-significant changes. These findings were in agreement with the results of the previous studies [28,33]. These non-significant changes may be resulted from the enhancement in antioxidant efficacies and erythrocytes protection of propofol against oxidative damage [34,35]. Moreover, it was reported that the propofol antagonize the effects of forced peroxidation of red cells at anesthetic and sub-anesthetic

concentrations [36]. There were no significant changes in other measured blood constituents such as total serum protein, alkaline phosphatase activity, serum creatinine and blood urea nitrogen. These results were in accordance with what was recorded by Anandmay, *et al.* (2016) [28].

Generally, the results of the present study were in agreement with the results of the previous studies [28,37] regarding to the level of GGT which did not show any significant changes, but the use of 4mg/ kg b.w of propofol lead to significant increase ($P < 0.05$) in serum GGT activity only after recovery. It is well-known that Propofol is rapidly cleared by hepatic (mainly) and extrahepatic metabolism. It is metabolized by glucuronide conjugation in liver. The transient increase in GGT level with dose of 4mg/kg might be due to hepatic stimulation after propofol administration. This group was the first treated group that received for the first time the propofol. The authors in the present work postulated this transient increase of GGT may occur with any dose of propofol (low or high), provided that the animals receive the drug for the first time. The subsequent administration of propofol (in the second and third groups) may not lead to any significant changes.

The results of the present study revealed that 4mg/ kg b.w of propofol lead to significant decrease in serum total cholesterol and LDL levels ($P < 0.05$) after administration and recovery. These results were unlike the results reported before [38]. In that study HDL-cholesterol concentrations tended to be greater in patients receiving propofol. However, 6 and 8 mg/kg b.w of propofol did not cause any significant difference in the serum lipid concentrations which was similar to what was recorded by Gottardis, *et al.* (1989) [39].

Conclusion

According to the results of this study, it could be concluded that the use of different doses of propofol (4, 6 and 8 mg/kg) has a little effect on different physical, hematological and biochemical parameters. These changes may appear in animals received the propofol for the first time. The different doses of propofol mostly result in the same anesthetic effect regarding the onset, duration, and recovery. The propofol which was preceded with xylazine-ketamine gives rapid onset, smooth recovery of anesthesia but with a duration ranged from 20 - 30 minutes. The increase of propofol dose did not affect the onset or duration of anesthesia but may be associated with major side effects especially the respiratory depression and apnea. It is recommended that the use of a dose of 4 mg/kg of propofol in premedicated animals provided that injection of propofol should be carried out slowly which may prolong the duration of anesthetic effect and lower the detrimental effects such as respiratory depression and apnea.

Conflict of Interests

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