Alexandria Journal of Veterinary Sciences
www.alexjvs.com

AJVS. Vol. 57 (1): 106-114. April 2018
DOI: 10.5455/ajvs.290272

Clinical Evaluation of Intravenous Propofol Alone or in Combination With Diazepam, Ketamine Hcl and Thiopental Sodium to Induce General Anaesthesia in Dogs

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Key words:
General anesthesia, propofol , diazepam, ketamine, thiopental, anaesthetic combinations, dogs.

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ABSTRACT

This study aimed to evaluate hemato-biochemial and clinico-physiological effects addition to the anesthetic properties of propofol alone or in combination w diazepam, ketamine Hcl or thiopental sodium. For this purpose, 12 apparently heal male dogs were randomly divided into four equal groups; A, B, C and D. All dc were permedicated with xylazine Hcl (1mg/kg Bwt/IM) then intravenous anesthe was induced in group A with(5 mg/kg Bwt)propofol or with propofol and ketam hydrochloride mixture(2mg/kg Bwt of each drug in group B ,or with propofol a thiopental mixture (2.5 mg/kg propofol and 6,5 mg/kg thiopental) in group c wh group D receveid propofol (2mg/kg Bwt) followed 0.2mg/kg Bwt diazepam. Blc samples were collected from the four groups 15 minutes before anesthesia inducti then at (15, 45, 75 and 120) minutes after treatments for the hemato-biochemi evaluation, also clinico-physiological observations were recorded at the same previc times. A slight alterations in some physiological parameters and hemato-biochemi values was observed after anesthesia induction in the four groups, but it still safe induce general anesthesia in dogs. However propofol –thiopental mixture shov longest anesthesia duration with complete muscle relaxation and sedation that suitable for most surgical operations.

1. INTRODUCTION

thiopental, propofol, and ketamine are Injectable general anesthetic agents used for induction of anesthesia in the healthy dog .also it may administered in combination with diazepam to reduce the quantity needed and improve the quality of induction (McClune et al., 1992).

Propofol –thiopental mixture showed benefits of reduced pain on injection, stability, reduced support of bacterial growth .Moreover the mixture induce a rapid smooth anesthesia, and absence of effect upon recovery profile (Prankerd *and Jones*, 1996). Propofol is an exclusive non-barbiturate, non-steroid,short-acting general intravenous anaesthetic agent and may cause hypotension and apnea. Propofol is often chosen for patients with hepatopathy and for those where a rapid recovery is desirable (Stoelting, 1999). ketamine-propofol combination has some advantages such as limited incidence of propofol induced respiratory depression, provision of analgesia from the ketamine and decrease the cardiorespiratory side effects (Mair *et al*., 2009) over using ketamine or propofol alone. Anaesthetic duration of propofol may be improved when it combined with premedication like diazepam which is a well-known benzodiazepine derivative used in various animal species. It was stated to have a minimum effect on respiratory system, heart rate and rectal temperature. Also it expected to cause good muscle relaxation and may be used to control convulsions. Still, studies on this combination are rare (Suresha et al., 2012). No single anesthetic agent provides all of the components of general anesthesia without affecting some vital organ function. Therefore a multiple drug technique (balanced anesthesia) is exploited to reduce sensory, motor,

sympathetic and parasympathetic reflex activities, and to diminish individual components of the anaesthetic state (Potliya et al., 2015). The aim of this study is to evaluate the efficacy and safety of propofol and propofol combination with diazepam, ketamine Hcl and thiopental sodium for general anesthesia induction in dogs. Also determine the most efficient and safest combination for induction of sedation and analgesia with the least adverse effects on clinicophysiological and haematological parameters.

2. MATERIALS AND METHODS

Twelve apparently healthy adult male dogs with mean weights of (25±5) kg and mean age of (10±5) months- were used in the current study

2.1. Study design:

The animals were divided randomly into four groups each of 3animals. The animals in each group were premedicated with injection of xylazine HCl (Xyla-Ject, Adwia Co., S.A.E 10th Ramadan City, Egypt.), 1mg/kg Bwt/IM **(**Muir et al., 1977). Then 15 minutes later dogs in group A were injected with 5mg/kg Bwt propofol (Propofol-lipuro10mg B.Braun Meslugan AG Germany) (Saikia et al., 2016) .While in group B dogs were injected with propofol-ketamine mixture at dos of 2 mg/kg Bwt of each drug (ketamine500mg, Sigma-Tec pharmaceutical industries)& (Propofol-lipuro10mg B.Braun Meslugan AG germany)according to (Saikia et al., 2016) . while dogs in group c received a mixture of Thiopental (500mg EPICO,Egypt) and propofol (Propofol-lipuro10mg B.Braun Meslugan AG germany) in a dose of 2.5 mg/kg propofol and 6.5 mg/kg thiopental equivalent to 0.5 ml/ kg of the mixture (Larisa et al ., 2008).the dogs in the last group received propofol (2mg/kg Bwt)followed 0.2mg/kg Bwt diazepam(neuril 10 mg 2ml, memphis pharmaceutical and chemical industries,Egypt)as co-induction agent (Fayyaz et al ., 2009).

2.2. Animals preparation to anesthesia:

The animals were fasted for 12 hours prior to anesthesia with free access to water. The area over the cephalic vein was clipped and shaved with manual shaver, then the skin sterilized by using ethyl alcohol as antiseptic for aseptic injection, and then Placement of an intravenous cannula (22 gauge and 33ml/min – Euromed medical industries, S.A.E., Cairo, and Egypt.) was carried out for blood sampling and drug administration. Dose calculation was carried out according to the preliminary study on the drug concentration and animal weight as recorded before.

2.3. Assessment of anesthetic parameters: The anesthetic effect of the four protocols were evaluated through determining of the onset of anesthesia (time from induction till loss of sensation and body reflexes and anesthesia duration (time from loss of sensation and regaining the sensation and body reflexes). Also the absence and regaining of certain body reflexes was observed as corneal reflex , pupil reflex ,plaperal reflex, Mandibular tone reflex, Tongue pinch reflex, ear pinch reflex, tail, Anal reflex, Tail flaccidity, toe pinch reflex ,patellar reflex. Evaluation of recovery depended observing the return of reflexes and recording Time to first head lifting.Moreover dogs are observed for any behavioral changes for example: Hypersalivation , Neurologic signs, Vomiting and urination.

2.4. Blood sample collection: Venous blood samples were collected in vials containing EDTA, for hematological determination of RBCs,WBCs, Hemoglobin content (HB %), Hematocrit (HCT) and Platelets (PLT) 15 minutes before anesthesia induction at 15, 45, 75 and 120 min after drug administration. Part of blood were collected in plain tubes, for detection of the level of Glucose, Cholesterol,creatinine ,blood urea nitrogen ALT and AST (Fig. 1).

2.5. Clinico-physiological observation: The clinical observation of the following parameters was recorded 15min before and 15, 45, 75 and 120 min after anesthesia inductio. The heart rate was measured as beats/min via auscultation (Ko et al., 2006). Respiratory rate (RR), measured by observing the movement of the thoracic wall motion per minute (Lemke et al., 2002). Rectal temperature measured with a digital thermometer (Medlink,hambrug - Germany).

Fig (1) showing the time of administration of preanesthetic and general anesthetic drug in addition to blood sample collection and and clinicophysiological observations (heart rate, respiratory rate, temperature) time.

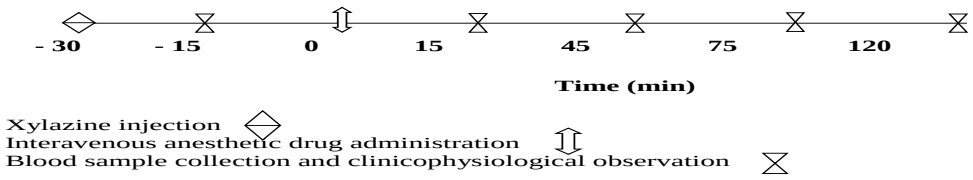

Fig (1): showing the time of administration of preanesthetic and general anesthetic drug in addition to blood sample collection and and clinico physiological observations (heart rate ,respiratory rate, temperature) tim

2.6. Statistical analysis

The data for parametric observations such as heart rate, respiratory rate and rectal temperature were analyzed using one-way analysis of variance (ANOVA) for comparison of means between the groups at corresponding intervals. The data were presented as the mean ± SD. Significance was accepted at $p < 0.05$.

3. RESULTS

3.1. General anesthetic effects: The determination anesthetic effects depended on three parameters include (onset of anesthesia or quality of induction, duration and recovery.

3.1.1. Onset of anesthesia: A significant difference was observed in onset and duration of anesthesia within the four groups. As propofol-ketamine group showed the most rapid onset of action (0.45±0.02 min) while propofol-diazepam group had the slowest onset of action (3.00±0.58 min) and the onset of anesthesia was quicker in propofol-thiopental group (1.00±0.05min) than propofol group (2.00±0.05 min) as in table (1).

3.1.2. Duration of anesthesia: Regarding to the duration propofol-thiopental mixture has the longest duration A (38.00±3.18) min while propofol – diazepam has the shortest durati

On (11.34±2.45 min), also It was observed that propofol (23.34±3.34) has longer duration than propofol –ketamine mixture (14.67±3.44) as in table (1).

3.1.3. Recovery:

The recovery in all groups was smooth, however convulsions and urination was observed during the recovery in dogs received propofol and diazepam. the complete recovery was recorded by observing the time of first sternal recumbancy ,head lifting and standing so dogs received propofol-thiopental has the longest recovery time while dogs in propofol – diazepam group has the shortest recovery time, and there was non-significant difference between propofol and propofol-ketamine groups as in table (2).

3.2. Clinico-physiological findings (pulse rate, respiratory rate and rectal temperature:

A significant decrease in rectal temperature was observed in the four experimental groups. Regarding to respiratory rate administration of propofol lead to a significant decrease but return to base line. While propofol-ketamine mixture resulted in a significant increase in respiratory rate. Also there was a fluctuation in respiratory rate in propofol-diazepam group but still above the base line .however injection of propofol-thiopental mixture didn't induce any significant change in respiratory rate. Concerning the heart rate it showed a significant increase in propofol and propofol-diazepam group. but in propofol-ketamine-group there was a significant increase that followed by a significant decrease then returned to its base line, while a fluctuation in heart rate was observed following propofol-thiopental mixture administration as in Table(3)

Table (1): Values of induction, duration after intravenous injection of propofol alone or in combination with diazepam, ketamine Hcl and thiopental sodium

Group	Onset	Duration
Propofol	2.00±0.05 B	23.34±3.34 B
Propofol/Ketamine	0. 45±0.01 D	14.67±3.44 C
Propofol/Diazepam	3.00±0.01 A	11.34±2.45 D
Propofol/Thiopental	1.00±0.05 C	38.00±3.18 A

Means within the same column of different litters are significantly different at ($P < 0.05$).

Table (2): Effect of propofol alone or in combination with diazepam, ketamine Hcl and thiopental sodium on time of first head lifting, time of sternal recumbancy and time of first standing.

Group	Time of first head lifting	Time of sternal recumbancy	Time of first standing
Propofol	43.33±1.67 B	60.00±4.51 B	91.67±3.71 B
Propofol/Ketamine	42.00±6.00 B	52.00±6.00 B	89.00±7.02 B
Propofol/Diazepam	32.33±4.37 C	44.67±3.18 C	80.00±5.77 C
Propofol/Thiopental	108.00±12.29 A	114.00±11.02 A	121.00±10.21 A

Means within the same column of different litters are significantly different at ($P < 0.05$).

Table (3): Effect of propofol alone or in combination with diazepam, ketamine Hcl and thiopental sodium on heart rate, respiratory rate and temperature before and after treatments.

Treatments	Time	Heart rate	Respiratory rate	Temperature
Propofol	Before treatment by 15 min	D 44.00±1.53	AB 17.33±1.76	A 39.33±0.09
	After treatment by 15 min	B 56.00±8.72	AB 18.00±1.53	B 37.80±0.36
	After treatment by 45 min	C 48.00±4.04	B 16.33±2.67	B 37.27±0.12
	After treatment by 75 min	C 52.33±8.09	D 12.67±1.45	B 37.17±0.17
	After treatment by 120 min	C 52.00±6.66	B 17.67±3.18	B 37.27±0.03
Propofol/ Ketamine	Before treatment by 15 min	D 44.00±5.29	C 14.67±1.86	A 39.13±0.38
	After treatment by 15 min	C 47.33±7.84	AB 17.00±3.06	B 37.40±0.36
	After treatment by 45 min	D 44.67±6.06	A 19.00±4.04	BC 36.93±0.18
	After treatment by 75 min	D 45.00±7.64	A 19.33±1.86	B 36.73±0.15
	After treatment by 120 min	D 42.00±9.54	B 16.00±2.08	BC 36.83±0.28
Propofol /Diazepam	Before treatment by 15 min	E 38.00±2.00	C 14.33±0.88	A 39.00±0.32
	After treatment by 15 min	D 42.00±4.16	B 16.00±2.08	B 36.37±0.62
	After treatment by 45 min	D 45.67±9.74	A 19.67±3.48	C 35.90±0.62
	After treatment by 75 min	C 49.33±12.60	B 16.67±0.33	C 35.63±0.64
	After treatment by 120 min	C 50.67±5.33	A 18.00±1.53	BC 36.27±0.45
Propofol/ Thiopental	Before treatment by 15 min	C 50.67±3.48	AB 17.00±1.15	A 39.40±1.04
	After treatment by 15 min	A 70.00±4.62	A 20.00±0.00	B 37.80±1.59
	After treatment by 45 min	B 57.67±3.18	A 18.67±1.45	B 37.10±1.78
	After treatment by 75 min	C 49.67±0.33	B 17.00±1.15	BC 36.53±1.78
	After treatment by 120 min	B 56.00±3.61	AB 17.67±0.88	BC 36.30±1.88

Means within the same column of different litters are significantly different at ($P < 0.05$).

3.3. Biochemical findings (Glucose, Cholesterol, ALT and AST, BUN, Creatinine): A significant increase was observed in glucose level throughout the experiment. A significant decrease was recorded in cholesterol level in propofol group while there was a significant increase in propofol-ketamine and propofol –thiopental and propofol diazepam groups.BUN showed a significant increase followed by a significant decrease and return to base line in propofol and propofol/ diazepam groups but in propofol-ketamine groups the significant decrease continued throughout the experiment while a slight

fluctuation was observed in propofol/ thiopental group as showed in table(4). There was non-significant in creatinine level in the four experimental groups throughout the experiment. Regarding to AST level a significant decrease was observed in propofol and propofol-thiopental group throughout the experiment. While the significant decrease in

Table (4): Effect of of propofol alone or in combination with diazepam, ketamine Hcl and hiopental sodium on Glucose, Cholesterol , BUN) before and after treatment

Treatments	Time	ALT (U/L)	AST (U/L)	Creatinine (mg/dl)
Propofol	Before treatment by 15 min	BC 34.43±1.86	A 52.20±3.18	AB 0.89±0.06
	After treatment by 15 min	B 38.37±2.16	A 52.83±3.95	AB 0.80±0.03
	After treatment by 45 min	B 38.17±1.58	B 48.30±4.20	AB 0.82±0.05
	After treatment by 75 min	B 38.45±2.09	B 44.40±2.05	AB 0.83±0.04
	After treatment by 120 min	B 37.94±1.96	B 49.84±5.66	B 0.71±0.11
Propofol/ Ketamine	Before treatment by 15 min	C 31.87±4.53	C 40.96±5.77	AB 0.93±0.10
	After treatment by 15 min	D 29.46±3.69	D 33.77±3.95	A 1.02±0.16
	After treatment by 45 min	BC 34.36±5.15	D 33.91±1.34	A 1.17±0.10
	After treatment by 75 min	B 40.66±6.99	D 34.18±4.24	A 1.08±0.11
	After treatment by 120 min	BC 35.60±4.18	C 38.18±3.82	A 1.11±0.11
Propofol/ Diazepam	Before treatment by 15 min	E 23.99±1.50	D 33.01±4.46	A 0.99±0.06
	After treatment by 15 min	B 39.08±10.62	E 27.01±2.97	A 1.00±0.19
	After treatment by 45 min	D 25.99±9.06	E 29.83±7.69	A 0.97±0.08
	After treatment by 75 min	C 32.07±5.07	D 35.57±5.83	AB 0.91±0.09
	After treatment by 120 min	B 39.85±6.50	C 41.30±6.53	A 0.99±0.07
Propofol/ Thiopental	Before treatment by 15 min	AB 50.08±21.27	B 46.30±6.91	A 1.11±0.13
	After treatment by 15 min	A 55.70±23.77	B 47.02±4.27	AB 0.93±0.06
	After treatment by 45 min	A 58.47±25.42	B 42.80±5.58	A 1.01±0.09
	After treatment by 75 min	A 56.98±24.34	C 38.39±4.19	A 0.99±0.09
	After treatment by 120 min	A 55.87±22.80	C 40.42±2.77	A 0.92±0.08

Means within the same column of different litters are significantly different at (P < 0.05).

AST after propofol-ketamine mixture administration followed by a significant increase were observed then returned to base line at the end of experiment. However a fluctuation was observed in propofol-diazepam group. Concerning ALT level there was fluctuation of ALT level was observed in propofol-diazepam group, as showed in table (5).

3.4. Hematological findings (RBCs, WBCs, Hb%, hematocrit, and platelets): A significant decrease in hemoglobin Hb % was observed in the four groups non-significant change in propofol and propofol-thiopental groups, while in propfol-ketamine group there was a significant decrease in ALT

Level followed by increase and returned to its baseline at the end of experiment, however a

after anesthetic agent administration; however red blood cells count RBCs showed non-significant change in propofol-thiopental group and decreased in the other experimental groups. A non -significant change in hematocrit was observed in the four groups

however a slight decrease was observed in propofol –thiopental group but return to the base line. A fluctuation in white blood cells (WBCs) and platelets count was observed in the four groups.as showed in table (6).

Table (5): Effect of of propofol alone or in combination with diazepam, ketamine Hcl and thiopental sodium on,(ALT and AST, Creatinine) before and after treatment:

Treatments	Time	BUN (mg/dl)	Glucose (mg/dl)	Cholesterol (mg/dl)
Propofol	Before treatment by 15 min	B 17.75±2.19	J 98.73±7.82	A 255.00±30.50
	After treatment by 15 min	A 18.15±1.88	H 123.70±11.46	B 243.00±22.37
	After treatment by 45 min	B 17.91±1.38	GH 129.00±2.52	B 245.00±21.52
	After treatment by 75 min	B 17.83±1.71	E 144.37±6.88	B 246.00±23.52
	After treatment by 120 min	B 17.73±2.26	FG 135.00±16.44	B 242.33±19.41
Propofol/ Ketamine	Before treatment by 15 min	B 17.50±2.02	K 82.77±6.73	D 188.67±20.95
	After treatment by 15 min	D 15.96±0.77	I 106.72±6.53	E 192.79±11.41
	After treatment by 45 min	E 14.49±2.53	D 154.38±16.26	D 197.82±13.42
	After treatment by 75 min	F 13.55±2.41	AB 188.72±32.73	C 211.45±15.20
	After treatment by 120 min	G 12.64±2.25	A 191.02±48.25	C 208.40±11.90
Propofol/ Diazepam	Before treatment by 15 min	C 16.93±0.95	I 109.73±17.69	J 134.86±26.10
	After treatment by 15 min	B 17.16±0.85	F 139.87±32.65	H 155.07±12.10
	After treatment by 45 min	C 16.38±1.03	C 167.50±48.52	H 158.37±18.98
	After treatment by 75 min	C 16.97±0.97	A 192.27±45.18	I 144.78±18.34
	After treatment by 120 min	C 16.05±2.79	B 182.97±43.68	G 164.32±13.24
Propofol/ Thiopental	Before treatment by 15 min	B 17.53±1.65	68.78±14.39	E 175.17±20.57
	After treatment by 15 min	D 15.20±1.82	I 103.27±20.05	F 182.37±21.10
	After treatment by 45 min	A 18.28±1.61	J 95.51±13.75	F 180.73±22.61
	After treatment by 75 min	B 17.93±1.77	J 99.86±17.32	F 181.50±22.16
	After treatment by 120 min	A 18.42±1.81	G 131.91±26.88	F 183.07±22.06

Means within the same column of different litters are significantly different at (P < 0.05).

4. DISCUSSION

Recent anesthetic practices recommend the combinations of drugs. This practice is known as a balanced anesthesia in which multiple drugs are used in low dosage as each drug is used for a specific purpose. The main purpose is to take advantage of the required characteristics of selected drugs while reducing their ability for undesirable depression of homeostatic mechanisms (Riviere and Papic, 2009).

In this study the anesthetic and the clinic-physiological effects of intravenous administration of propofol alone or in combination with diazepam, ketamine Hcl or thiopental sodium in addition to hemato-biochemical findings were evaluated. In the present study the onset of anesthesia induction in the four groups was rapid and smooth, however the dogs received propofol- ketamine showed the quickest onset of anesthesia while dogs received propofol - diazepam showed the slowest onset of anesthesia.

Also it was observed that the onset of anesthesia induction in dogs received propofol-thiopental was quicker than dogs received propofol alone. The current study showed that propofol-thiopental combination resulted in the longest anesthesia duration, while propofol-diazepam intravenous injection resulted in the shortest duration. Moreover, there wasn't a significant difference in the duration of anesthesia in propofol and propofol- ketamine group.

Table (6): Effect of propofol alone or in combination with diazepam, ketamine Hcl and thiopental sodium on (HB, RBCs, hematocrit, WBCs and platelets) before and after treatment:

Treatments	Time	Hb *(g/dl)*	RBCs ($x10^6$ /ul)	Hematocrit %	WBCs ($x10^3$ / ul)	Platelets $10^{\wedge 3}$/ul
Propofol	Before treatment by 15 min	C 13.03±1.07	B 5.30±0.55	AB 37.10±2.90	B 12.80±1.78	F 441.33±59.00
	After treatment by 15 min	D 12.13±0.76	C 4.93±0.37	B 34.43±3.00	D 10.47±0.38	G 427.33±60.67
	After treatment by 45 min	E 11.60±0.87	C 4.59±0.39	B 32.80±2.66	A 15.37±0.62	J 364.00±38.16
	After treatment by 75 min	D 12.60±0.78	C 4.15±1.06	B 30.00±7.16	F 8.23±2.58	H 416.00±69.97
	After treatment by 120 min	E 11.87±0.28	C 4.48±0.14	BC 28.10±4.04	D 10.03±1.49	H 394.00±86.67
Propofol / Ketamine	Before treatment by 15 min	A 15.37±0.79	A 6.38±0.51	A 45.53±3.35	C 11.53±0.90	H 416.33±88.68
	After treatment by 15 min	B 14.17±0.55	B 5.57±0.43	A 40.47±1.76	E 9.03±2.02	H 400.33±85.11
	After treatment by 45 min	B 14.37±0.90	B 5.34±0.37	AB 38.03±3.23	E 9.30±0.65	F 432.33±75.31
	After treatment by 75 min	B 14.17±0.83	B 5.74±0.38	A 41.00±1.64	D 10.57±2.57	H 413.67±75.33
	After treatment by 120 min	E 11.30±2.86	B 5.90±0.54	A 41.57±3.83	D 10.73±1.22	I 388.33±50.60
Propofol/ Diazepam	Before treatment by 15 min	C 13.23±0.38	A 6.07±0.49	AB 38.73±0.93	E 9.80±1.79	B 644.33±297.34
	After treatment by 15 min	E 11.90±1.39	B 5.50±0.77	B 34.77±3.96	D 10.40±4.39	D 582.67±259.69
	After treatment by 45 min	D 12.03±1.17	B 5.62±0.95	B 34.37±4.61	H 6.60±1.97	C 601.67±316.44
	After treatment by 75 min	E 11.60±1.52	B 5.47±1.10	B 33.87±4.68	H 5.80±1.96	E 544.33±391.93
	After treatment by 120 min	D 12.37±0.90	B 5.79±0.79	B 35.47±2.64	G 7.13±1.33	A 673.00±526.35
Propofol/ Thiopental	Before treatment by 15 min	B 14.23±2.22	B 5.85±0.79	A 42.83±6.12	E 9.90±0.91	K 246.67±20.28
	After treatment by 15 min	C 13.77±2.50	B 5.64±0.85	A 41.43±6.56	E 9.73±2.56	M 234.33±29.69
	After treatment by 45 min	D 12.79±2.15	B 5.26±0.67	AB 38.13±5.12	G 7.33±1.81	N 202.00±14.22
	After treatment by 75 min	D 12.83±2.13	B 5.35±0.78	B 39.03±5.98	F 8.07±1.83	L 244.33±30.55
	After treatment by 120 min	C 13.50±2.24	B 5.58±0.78	A 40.93±5.97	F 8.27±2.27	K 268.00±33.60

Means within the same column of different litters are significantly different at (P < 0.05).

The rapid recovery from ketamine is due to the poor binding to plasma protein (Ghoneim et al., 1997). The current results is compatible with Muhammad et al. (2009) who reported that Ketamine and propofol combination reduce the dose of propofol required for the induction of anesthesia. While the sedative and hypnotic effects of diazepam are negligible or absent in dogs as their bodies develops tolerance very quickly (Rankin, 2002). Our findings is incompatible with ko et al (1999) who found that combination of propofol and thiopental induced anesthesia of similar quality to propofol or thiopental alone and Recovery profile were similar to those of propofol and superior to those of thiopental. The findings of the current study may differ due to the breed and dose difference. A significant increase in

heart rate was observed in the four groups. this finding is similar to the result of Jolliffe et al. (2007) who found that Induction of anesthesia with propofol in dogs was associated with mild increase in pulse rate and Martinez-Taboada and Leece (2014) who observed that ketofol administration was associated with a greater increase in PR .the increase in heart rate may be due to sympathetic stimulation (Agrawal et al., 2012). Also Haskins et al. (1986) found that diazepam produced minimal cardiopulmonary effects, except for a significant increase in heart rate. Regarding to the respiratory rate a significant decrease was observed after propofol administration then returned to base line while it showed a significant increase in propofol-ketamine group and propofol diazepam group, however a non-significant change was observed in propofol-thiopental group.the bradypnea caused by propofol is likely due to the depression of the respiratory center and to the inhibition of the response to hypercapnea as mentioned by (Adetunji et al., 2002). Our findings is compitaple with Henao-Guerrero & Riccó (2014) who found that ketamine-propofol combination result in less respiratory depression than propofol alone due to the reduction in propofol dose. A significant decrease in rectal temperature was observed in the current study in the four groups this may be due to generalized sedation, decrease in metabolic rate, muscle relaxation (Zhang et al., 2012). This study showed a change in Hb, RBCs, WBCs and platelets count, also our results showed a decrease in ALT,AST.The decrease hemato-biochemical parameters during anesthesia or sedation may be due to shifting of fluid from the extravascular compartment to the intravascular compartment(Zhang et al., 2012). The blood cell count was diminished due to multiple and continued blood sampling, although the use of propofol was associated with greater decrease (Gronert et al., 1998). The observed increase in cholesterol may be due to the general response to stress or to altered metabolism as Lypolisis increases under the influence of catecholamines, and corticosteroids contribute to fat mobilization according to (Bush, 1991). While glucose level showed a significant increase in the four groups that may be a response to stress (Singh, 2003), or as result of hyperglycemic effect of ketamine or xylazine as (Saha et al., 2005).

5. CONCLUSION

The four protocols can be used for induction of general anesthesia in dogs, despite of slight physiological and biochemical changes.

Propofol-thiopental combination was showed the longest duration and smoothest induction and recovery, so it is suitable and advisable to be used in many surgical procedures of longer duration in dogs. Propofol-diazepam combination showed the shortest duration and convulsion during recovery, so it is not recommended to use for general anesthesia induction in dogs.

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