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Clinicophysiological and haematobiochemical effects of dexmedetomidine as preanesthetic in combination with thiopental sodium and ketamine in dogs

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Abstract
The objective of the study was to evaluate a safe anaesthetic protocol that could lead to fast and smoother recovery and to determine various clinicophysiological and haematobiochemical parameters before and after anaesthesia. Twenty four clinically healthy dogs of either sex were divided into four groups. Atropine sulphate was administered @0.04mg/kg IM in all the groups. In group 1 ketamine was administered intravenously @ 10 mg/kg body weight. In group 2, dexmedetomidine was administered @ 10 µg/kg body weight, intravenously followed by ketamine till effect. The animals of group 3 were subjected to the administration of thiopental sodium I.V till effect. In animals of the group 4 dexmedetomidine was administered @10 µg/kg I.V. and thiopental sodium given I.V till effect. Dexmedetomidine prior to administration of ketamine and thiopental sodium results in quicker induction, better analgesia for more duration and better muscle relaxation as compared to use of ketamine and thiopental sodium alone. Total dose of ketamine and thiopental sodium required to produce general anaesthesia was decreased in animals of group 2 and 4, with increase in duration of anaesthesia, prolonged recovery time and better muscle relaxation. The clinical efficacy of anaesthesia was determined by performing various surgical operation viz cystotomy, gastrotomy, spaying and entrotomy. Haematological and biochemical parameters showed variable changes at various time intervals.

Keywords: Thiopental sodium, ketamine, dexmedetomidine and dogs

Introduction
Use of sedatives prior to induction of anaesthesia improves the quality of anaesthesia and decreases the adverse effect of individual anaesthetic agent. Alpha-2 agonists have a major role in reducing the dose of subsequent anaesthetic agents. Dexmedetomidine is a potent and selective agonist of the α-2 adrenoceptor (Gerlach *et al.*, 2009) [11]. Dexmedetomidine, an α_2-adrenoreceptor agonist is becoming increasingly popular in veterinary practice to facilitate the examination and surgical manipulation of small animals primarily due to its rapid onset of sedation and analgesia. Dexmedetomidine has been evaluated in the dog alone and in combination with several other drugs viz. diazepam, butorphanol and ketamine (Granholm *et al.*, 2007) [13]. Ketamine is a non-barbiturate, non-narcotic agent and when administered parenterally produces catalepsy of short duration (McCarthy and Chen, 1965) [25]. Ketamine has been recommended for anaesthesia of critically ill patient in which there is a risk of cardiac depression and hypotension (Smith *et al*., 1979) [33]. Ketamine is used largely in dogs (Wilson *et al*., 2008; Aguado *et al*., 2011) [40, 2] However ketamine does not provide adequate muscle relaxation and analgesia (White *et al*., 1982) [39]. Thiopental sodium is a powerful hypnotic that produces dose-dependent depression of the central nervous system (CNS). The doses of barbiturate may be reduced with pre administration of alpha-2 agonist Jadon *et al.* (1998) [15].
The purpose of this study was to elucidate the clinical, physiological, and haematobiochemical effect of α-2 agonist agent dexmedetomidine with and without ketamine and thiopental sodium in dogs.

Materials and Methods
Twenty four dogs of either sex, ranging from one to five year of age and 15 to 20 kg body weight were randomly divided into 4 groups viz., Group 1, 2, 3 and 4, comprising of 6 animals in each and observed for the effect of different anaesthetic regimen on clinical, physiological, haematological and biochemical parameters. The food and water was withheld for 12 hour and for 6 hours respectively prior to administration of anaesthetic drugs. The animals of all the groups were premedicated with atropine sulphate @ 0.04 mg/kg body weight intramuscularly.

Ten minute later ketamine hydrochloride was administered @ 10 mg/kg body weight intravenously in group 1. In group 2 combination dexmedetomidne @ 10µg/kg body weight and ketamine hydrochloride was administered intravenously to the effect at 5 min. interval. The animals of group 3 were premedicated with atropine sulphate @ 0.04 mg/kg body weight intramuscularly followed 10 minutes later by thiopental sodium (2.5%) intravenously till effect. In group 4 atropine sulphate was given as in group-3 followed 10 minutes later by dexmedetomidne @ 10 µg/kg body weight intravenously and thiopental sodium (2.5%) intravenously till effect 10 minutes after dexmedetomidine administration.

The clinical efficacy of the anaesthesia was assessed by observing onset of anaesthesia, duration of anaesthesia, complete recovery time and surgical operation viz cystotomy, gastrotomy, spaying and entrotomy. Physiological parameters heart rate, respiration rate and rectal temperature. Haematological parameters viz. haemoglobin (Hb), packed cell volume (PCV), total erythrocyte count (TEC), total leucocyte count (TLC) and differential leucocyte count (DLC) were estimated as per the procedure described by Schalm *et al.* (1975) [30]. Level of biochemical parameters viz. serum glucose, total protein, blood urea nitrogen, creatinine, alanine aminotransferase and asparate aminotransferase and electrolytes like sodium, potassium, chloride, were estimated by using semi-automatic biochemical analyzer.

Blood samples were collected before atropine administration (0 minute) and at 10, 30, 60, 120 minute, 6hr, 24hr, 48hr interval after administration of drugs. Blood (2ml) was collected in clean glass vial containing 3mg of ethylene diamine tetra-acetic acid (EDTA) for estimation of haematological parameters while 3ml of venous blood was collected at above mention time interval, in sterilised dry test tube for the collection of serum which was kept under refrigeration at -20 ºC.

The statistical analysis was done using analysis of variance (ANOVA), as per the procedure described by Snedecor and Cochran (1980) [34].

Result and Discussion

Preanaesthetic administration of dexmedetomidine (10 µg/kg i.v.) reduced the desired dose of ketamine from 10 mg/kg to 3.17±0.15 mg/kg body weight**.** The reduction in the dose of ketamine may be due to addidative sedative effect of dexmedetomidine. Similar observation has been reported by Ahmed *et al.* (2013) [3] after the use of dexmedetomidine and ketamine in dogs. The mean±SE dose of thiopental sodium to produce the desired effect was 15.21±0.31 mg/kg body weight in animals of group3, however, it reduced to 6.23±0.18 mg/kg body weight in animals of group 4.This decrease in the dose of barbiturate may be due to sedation potentiating effect of dexmedetomidine. Similar observations in the reduction of barbiturate dose have been reported by Jadon *et al*. (1998) [15].

The duration of onset of anaesthesia was 15.77±0.44 min. and 38.47±0.71 min. in the animals of group 1 and 2 respectively. Complete recovery was 45.11±2.23 min. and 53.11±3.63 min. in the animals of group 1 and group 2 respectively. The time taken for recovery was longer in group 2 as compared to group 1. Increase in duration of anaesthesia has also been reported by Posner and Burns (2009) [26] and Barletta *et al.* (2011) [6] in the dogs after ketamine-dexmedetomidine anaesthesia. The increase in the duration of anaesthesia and recovery time may be due to additive sedative effect of dexmedetomidine Granholm *et al.* (2007) [13].

The duration of anaesthesia was significantly ($P<0.01$) higher in animals of group 4 (20.62±0.33 minutes) as compared to animals of group 3 (8.08±0.38 minutes).Complete recovery was observed in 34.98±1.62 min and 58±2.26 min. in animals of group 3 and 4, respectively. Longer recovery time in group 4 as compared to group 3 may be due to the additive effect of thiopental sodium with α_2-agonists (Jadon *et al*., 1998) [15].

There was increase in heart rate in the animals of group 1 at 5 to 60 min. time interval, (Table-1a) whereas in the animals of group 2, heart rate was increased significantly at 15 to 30 min. time interval and return near to normal level at 90 min. interval. A significant tachycardia was observed in group 1 and group 2 which might have been due to cardiovascular stimulating effect of ketamine. It is mainly due to its action on sympathetic trunk. Heart rate and cardiac output increased due to myocardial stimulation by ketamine in group 1, while in group 2 dexmedetomidine initially caused bradycardia followed by tachycardia after administration of ketamine,. The bradycardia due to dexmedetomidine has been attributed to vagal activation by alpha 2 adrenoceptors, potential pre-functional alpha 2 inhibition at cardiac pacemaker tissues and involvement of baroreceptor reflex under alpha 2 adrenoceptor agonist (Sarzan *et al*., 1989) [29].

Heart rate increased gradually and significantly ($p<0.01$) increased in the animals of group 3 and 4 for 60 min. and 15 min. respectively with peak level of 123.33±1.46 observed at 30 min. interval. Venn *et al.* (2000) [38] reported that dexmedetomidine subside hypertension and tachycardia. Similar observation have also been reported by Joubert and Lobetti (2002) [16] in dog under medetomidine-thiopental sodium anesthesia.

There was a non significant decrease in respiration rate (Table-1a) in the animals of group 1, however, in the animals of group 2, a significant decrease in respiration rate at 5 min to 60 min. interval was observed which returned to near normal level at 90 min. interval in both the groups of animals. Ketamine does not depress ventilator responses. In dogs anaesthetized with ketamine, respiratory and minute volume decreases initially but both return to base values within 15 minutes (Haskin *et al.*, 1985) [14]. Respiratory depressant effect of the alpha 2 adrenergic agonists are likely to be exaggerated when used in combination with other anaesthetic and analgesic agents (Sindak *et al*. 2010) [31], and Amarpal *et al*. (2013) [4] have also reported decrease in respiration rate after administration of ketamine and alpha-2 agonist in dogs.

There was a gradual and non-significant decrease in rectal temperature (Table-1a) in both the groups of animals after the administration of different drug combinations which returned near base level at 90 min. interval in both groups. The slight hypothermic response might be due to peripheral vasodilation as a consequence of increase vagal tone (Lyon 2000 and Amarpal *et al*. 2013) [23, 4].

A gradual and significant ($p<0.01$) decrease in respiration rate and rectal temperature was observed in animals of group 3 and group 4 upto 30 min. Respiration was at its lowest level of 15.33±0.46 at 30 min. interval in group 3 and 11.17±0.72 at 15 min. in group 4 as compared to base value of 31.33±1.12 and 26.67±1.32 in group 3 and 4, respectively. Temperature was at its lowest level of 37.28±0.33 at 15 min. interval in group 3 and 37.97±0.42 at 30 min. in group 4 as compared to base value of 38.46±0.41 and 38.82±0.31 in group 3 and 4, respectively. Decrease in respiration rate might be attributed to the combined effect of systemic administration of dexmedetomidine and barbiturate (Sabbe *et*

al., 1994) [27]. The decrease in respiration rate observed in present study confirms the finding of Lerche and Muir (2004). Dexmedetomidine has been reported to activate α-2 receptors which lead to decrease in rectal temperature (Lemke, 2007).

There was a gradual and non significant decrease in haemoglobin level in both the groups of animals. A significant decrease in PCV level in the animals of group 1 at 10 min. interval was observed, which remained below normal till 6 hrs interval. In the animals of group 2, the PCV level gradually and significantly decreased at 60 min. interval. The level of TEC (Table-1b) decreased in both the groups. A significant decrease in the value of TEC was observed in the animals of group 1 at 20 min. to 6 hrs interval and at 30 to 60 min. interval in group 2. Decrease in haemoglobin (Hb), packed cell volume (PCV), and total erythrocyte count (TEC) in both the groups at various time intervals may be attributed to the pooling of blood cells in the spleen, induced by the adrenolytic property of alpha 2 adrenoceptor drugs and dissociative anaesthetic agents. However, it may be noted that the decrease in these parameters was transient and returned near the preadministration levels at 48 hrs interval. Similar changes have been observed in haemoglobin, total erythrocyte count and packed cell volume levels after administration of alpha 2 adrenoceptor agonist and ketamine in dogs by Amarpal *et al*. (2013) [4] and Umar and Adam (2013) [37].

A significant (P<0.01) decrease in haemoglobin, PCV and total erythrocyte count observed in animals of group 3 and 4 at various time intervals may be attributed to the pooling of blood cells in the spleen which is induced by the adrenolytic properties of α_2-adrenoceptor and barbiturate (Table-2a). However, decrease in these parameters were transient and returned to pre-administration level by 24 to 48 hours in both the groups. Similar changes have been observed in haemoglobin, total erythrocyte and packed cell volume level after administration of α_2-adrenoceptors agent in dogs by Skarda and Muir (1996).

The level of TLC decreased in the animals of group 1 after the administration of ketamine upto 60 min. interval, however, in the animals of group 2 the TLC level increased non significantly (p>0.05) upto 60 min. interval. There was a non significant increase in neutrophils level in the animals of group 1 and group 2 up to 60 min. interval. Insignificant fluctuating changes in monocytes, basophils and eosinophils were observed in both the groups of animals which reached near normal level at 24 to 48 hr interval. A non significant and transient increase in the total leucocyte count with corresponding lymphocytopaenia observed between 30 minutes to 12 hours in group 2 may be attributed to stress and release of ACTH on account of their administration. While non-significant decrease in group 1 may be due to minimal effect on haemodynamic parameters (Lerche *et al*., 2000) [22]. Similar observation has been reported by Bayan and Konwar (2014) [21] after administration of α_2 agonist drugs in dogs. A non-significant and transient increase in differential leucocyte count in 3 and 4 groups may be due to stress and release of ACTH on account of their administration (Felsner *et al*., 1995) [10]. Basophils, eosinophils and monocytes showed insignificant fluctuating changes in both groups of animals.

In group 1 significant increase in the value of glucose (Table-1b) was observed with peak level at 60 to 120 min. interval. In animal of group 2 gradual and insignificant increase was observed till 60 min. interval. The level of glucose reached near base value at 48 hr interval in both the groups. Elevated sugar levels have been correlated with increase in cortisol level. Under stressful condition especially during anaesthesia, there is an increased liberation of glucocorticoid, which could be responsible for the rise in glucose level. Administration of alpha 2 agonist activate alpha 2 receptors on pancreatic beta cells and inhibit release of insulin for approximately 2 hours (Ambrisko and Hikasa, 2002) [5].

A gradual and significant (p<0.01) increase in glucose level was observed in animals of 3 and 4 groups upto 120 min, Its level has reached near normal by 24 to 48 hrs in both the groups (Table-2a). The level of glucose was higher in animals of group 3 as compared to animals of group 4 at various time intervals throughout the period of study. Increase in blood glucose level might be attributed to the effect of α-2 adrenoceptor agonists that was associated with growth hormone stimulation and insulin suppression through direct inhibitory effect of dexmedetomidine on the pancreatic β-cells (Dollery, 1991) [9]. Low insulin activity causes inhibition of serum glucose utilization that lead to rise in serum glucose level (Surbhi *et al.*, 2010) [36].

A non significant (p>0.05) transient decrease in the level of total protein(Table-1b) was observed in both the groups. The decrease in total protien level may be due to haemodilution. Similar findings have been observed after administration of ketamine with alpha-2 agonist in dogs by Umar and Adam, (2013) [37] and Mazumdar *et al.* (2015) [24]. Level of BUN increased significantly in group 1 and non significantly in group 2 (Table-1b) whereas serum creatinine increased non significantly in both the groups. (Table-1b) A significant increase in serum urea nitrogen and creatinine may be due to temporary inhibitory effect of drugs on renal blood flow and consequent decrease in glomerular filtration rate, resulting in the rise in their level. Ketamine alone causes a significant increase in creatinine and blood urea nitrogen. Similar observation has been reported by Sadik *et al*. (2012) [28].

A gradual and non-significant decrease in total protein level in the animals of 3 and 4 groups upto 60 min. Might due to inter compartmental fluid shift causing haemodilution. Blood urea nitrogen level and serum creatinine level increased significantly upto 60 min in the both the groups, However more significant (p<0.01) increased was observed in animals of group 3 compare to group 4 (Table-2a). It may be due to temporary inhibitiory effect of alpha-2 agonist and barbiturate on renal blood flow and consequent decrease in the glomerular filtration rate, resulting rise in its level. It may also be due to increased level of anti-diuretic hormones (Church *et al*., 1994) [8].

A non significant (p>0.05) increase in the level of ALT and AST(Table-1b) was observed in both the groups of animals at different time intervals. The AST and ALT value returned near normal level after 48 hr in both the groups of animals. When liver damage occurs, then its membranes may become permeable or wall may rupture so that enzyme diffuse into the blood stream and resulted increase in level of alanine aminotransferase and aspartate aminotransferase in the blood circulation. The cytoplasmic enzymes such as alanine aminotransferase and aspartate aminotransferase are affected by the permeability of the cell membrane and their increase indicates liver damage (Abou-Ghanema *et al.* 2014) [1].

ALT and AST level significantly increased (p<0.01) in animals of 3 and 4 the groups and reached normal physiological limit within 48hr in animals of both the groups (Table-2a). Increase in level of ALT and AST may be attributed to the damage resulting into the membranes becoming more permeable or wall may rupture, so that the

enzyme diffuse into the blood stream and its level is increased in the blood circulation (Koichev *et al*., 1988) [18].

A non significant (p>0.05) and transient decrease in the level of serum sodium and potassium was observed in both the groups of animals. A transient short term decrease in the serum potassium level may be due to the entry of potassium into cells or increased level of minerals, corticosteroids in conjugation with the action of insulin (Kim and Jang, 1999) [17]. The changes in level of sodium may be related with disturbances in electrolyte metabolism, alteration in homeostasis and the effect on renin angiotensin system (Kim and Jang, 1999) [17]. The various surgical operation viz cystotomy, gastrotomy, spaying and entrotomy were performed under the ketamine and the combination of alpha-2 agonist and ketamine. The extent of muscle relaxation, sedation and analgesia was better in the animals of group 2 as compared to the animals of group 1. The surgical operation was performed smooth without any complication in the animals of group 2.

A transient and insignificant increase in serum sodium (Table-2a) in animals of 3 and 4 groups in the present study may be related with the disturbances in electrolyte metabolism, alteration in homeostasis and the effect on renin-angiotensin system (Stevenson, 1960) [35]. A gradual decrease in serum potassium level upto 60 min. (Table-2a) wsa observed in animals of both the groups which reached its base value by 24 to 48 hr. A transient short term decrease in serum potassium level may be due to entry of potassium into cells or increased level of mineral corticoids (Gill, 2004) [12]. A gradual and significant (p<0.01) decrease in serum chloride level upto 60 min. in animals of both groups may be attributed to respiratory depression in response to intravenous administration of α-2 adrenoceptor agonists, as chloride level is affected due to change in respiratory activity.

On the basis of above mentioned parameter it was observed that dexmedetomidine premedication prior to administration of ketamine and thiopental sodium results in quicker induction, better anaesthesia for prolonged duration with better muscle relaxation as compared to use of ketamine and thiopental sodium alone. Preanaesthetic administration of dexmedetomidine (10 µg/kg i.v.) reduced the dose of ketamine from 10 mg/kg to 3.17±0.15 mg/kg intravenously and thiopental sodium from 15.21±0.31 mg/kg body weight in animals of group3 to 6.23±0.18 mg/kg body weight in animals of group 4.

Table 1 a : Mean±SE of physiological parameters after administration of ketamine with and without dexmedetomidine in different groups of animals at different time intervals**.**

Parameters (Mean±SE)	group	0min	5min	15min	30min	60min	90min
Heart rate (Beat/min)	1	103.67±4.93	122.33±3.76*	135.83±1.64**	141.67±1.51**	121.50±4.95	112.8±34.73
	2	102.33±2.52	108.33±4.54	121.17±1.56**	123.83±4.02**	107.67±1.97	106.33±2.15
Respiration rate (/min)	1	27.83±1.25	24.50±1.22	24.30±1.94	26.33±0.83	27.00±1.36	27.67±1.38
	2	28.83±1.25	16.67±1.01	14.17±0.82	17.00±1.47	20.67±1.08	23.50±1.46
Rectal temperature (^{0}C)	1	39.96±0.18	39.74±0.18	39.15±0.13	39.02±0.14	39.78±0.13	39.73±0.14
	2	39.63±0.15	39.18±0.19	39.32±0.20	39.07±0.22	38.93±0.23	39.77±0.18

* Significant at p<0.05 difference with 0 min time interval

** Significant at p<0.01 difference with 0 min time interval

Table 1 a: Mean±SE of heamtobiochemical parameters after administration of Ketamine with and without dexmedetomidine in different groups of animals at different time intervals.

		Time intervals							
Parameters (Mean±SE)	group	0min	10min	30min.	60min.	120min	6hr	24hr	48hr
Haemoglobin(gm/dl)	1	12.30±0.63	12.05±0.54	11.81±0.47	11.80±0.54	11.99±0.61	11.88±0.69	12.00±0.64	12.24±0.64
	2	12.33±0.38	12.18±0.36	11.84±0.26	11.84±0.30	12.15±0.38	12.21±0.37	12.23±0.38	12.28±0.37
PCV (%)	1	37.27±1.30	34.30±1.09*	32.71±1.15**	32.25±1.25*	32.65±1.55**	33.52±1.60**	34.51±1.67*	36.35±1.48
	2	41.21±0.48	40.49±0.37	38.82±0.86	37.96±0.75*	39.84±0.63	39.92±0.58	40.20±0.49	40.56±0.43
TEC (10^6/µl)	1	6.00±0.24	5.61±0.12	5.17±0.21*	4.94±0.27**	5.12±0.36**	5.29±0.37*	5.71±0.30	5.80±0.0.33
	2	6.31±0.42	5.70±0.45	5.41±0.47*	5.21±0.43*	5.54±0.49	5.68±0.49	5.79±0.49	5.97±0.43
TLC(10^3/µl)	1	14.22±0.49	13.74±0.21	13.30±0.36	13.07±0.49	13.52±0.24	13.58±0.7	13.71±0.20	14.13±0.40
	2	13.08±1.07	13.43±1.45	13.93±1.38	13.81±1.40	13.80±1.40	13.44±1.38	13.25±1.40	13.02±0.74
Glucose(mg/dl)	1	80.94±2.85	86.50±2.33	94.68±3.62*	100.13±2.85**	103.55±3.47*	93.62±2.29*	87.02±2.48	82.30±3.09
	2	83.10±1.86	85.41±2.11	88.18±2.98	93.16±1.91*	90.78±2.54	88.25±3.32	84.00±2.77	83.24±2.76
Total Protein(g/dl)	1	6.72±0.12	6.41±0.11	6.21±0.07	6.12±0.07	6.19±0.06	6.40±0.09	6.63±0.13	6.66±0.12
	2	6.33±0.16	6.00±0.16	6.03±0.19	5.77±0.21	5.82±0.21	5.94±0.21	6.18±0.18	6.27±0.17
Blood urea nitrogen(mg/dl)	1	21.50±0.82	21.63±0.62	23.78±0.66*	24.30±0.82*	23.86±0.66*	23.47±0.67	20.48±0.82	21.50±0.81
	2	21.25±0.97	21.51±0.95	21.71±0.94	21.81±0.92	21.62±0.90	21.52±0.90	21.42±0.94	21.33±0.96
Creatinine(mg/dl)	1	0.75±0.04	0.81±0.04	0.89±0.04	0.93±0.02	0.87±0.04	0.81±0.03	0.76±0.04	0.75±0.03
	2	0.98±0.09	1.02±0.10	1.14±0.16	1.17±0.17	1.05±0.10	0.98±0.07	0.96±0.07	0.98±0.09
Sodium(mEq/dl)	1	140.44±2.91	139.73±1.96	139.62±1.95	139.49±1.96	140.67±2.72	139.60±2.03	140.00±2.06	140.11±2.13
	2	140.28±1.45	138.92±1.48	138.49±1.48	138.31±1.47	139.07±1.47	138.62±1.45	138.36±1.45	138.33±1.46
Potassium(mEq/dl)	1	5.16±0.36	4.98±0.56	4.64±0.43	4.55±0.42	4.59±0.43	4.72±0.40	4.95±0.27	5.08±0.34
	2	5.27±0.21	5.22±0.23	5.17±0.19	5.14±0.22	5.32±0.22	5.38±0.38	5.28±0.38	5.30±0.37
Chloride(mEq/dl)	1	104.94±4.25	109.54±4.41	110.46±4.66	110.74±4.75	110.61±4.50	109.46±4.28	105.28±4.26	104.27±4.27
	2	103.63±1.37	103.81±1.31	103.88±1.26	103.98±1.23	103.92±1.14	103.71±1.26	103.66±1.32	103.28±2.74
AST (IU/L)	1	103.63±1.37	103.81±1.31	103.88± 1.26	103.98± 1.23	103.92 ±1.14	103.71±1.26	103.66±1.32	103.28±2.74
	2	39.99± 2.81	40.16±2.79	40.33± 2.80	44.44± 2.80	40.32±2.81	40.15± 2.81	40.07± 2.82	40.00± 2.82
ALT(IU/L)	1	42.28± 0.45	45.32± 1.39	45.81± 2.11	46.68± 2.06	46.70 ±1.05	43.06± 0.63	42.67± 0.50	42.21 ±0.44
	2	40.87± 0.86	41.21± 0.94	41.46± 0.91	41.67± 0.90	42.29 ± 1.05	42.05 ±1.09	41.32± 0.97	41.20± 0.93

* Significant at p<0.05 difference with 0 min time interval

** Significant at p<0.01difference with 0 min time interval

Table 2b: Mean ± SE of heamtobiochemical parameters after administration of thiopental sodium with and without dexmedetomidine in different groups of animals at different time intervals.

Parameters (Mean ± SE)	group	Time intervals							
		0min	10min	30min.	60min.	120min	6hr	24hr	48hr
Haemoglobin(gm/dl)	1	11.43±0.31	11.26±0.27	10.53±0.29*	10.55±0.29**	11.02±0.17	11.03±0.21	11.37±0.25	11.41±0.24
	2	11.45±0.27	11.32±0.27	10.51±0.45**	10.61±0.4*	11.14±0.26	11.29±0.26	11.36±0.27	11.40±0.28
PCV (%)	1	41.99±1.23	41.48±1.19	40.63±1.22	39.94±1.38*	40.06±0.77	40.19±0.71**	40.67±0.75	41.12±0.77
	2	41.59±0.57	41.29±0.59	40.15±0.61	40.03±0.67	40.80±0.74	41.12±0.48	41.51±0.57	41.56±0.57
TEC (10^6/µl)	1	4.67±0.09	4.62±0.09	4.21±0.04**	4.17±0.03**	4.38±0.14**	4.53±0.1	4.56±0.1	4.61±0.09
	2	5.57±0.15	4.98±0.28**	4.66±0.32**	4.63±0.31**	4.79±0.28**	4.93±0.27	5.19±0.3	5.22±0.31
TLC(10^3/µl)	1	11.92±0.71	12.47±0.67	12.62±0.69	12.75±0.68	12.97±0.67	12.61±0.7	12.49±0.65	12.17±0.63
	2	10.11±0.09	10.42±0.09	10.87±0.11	10.73±0.09	10.86±0.09	10.79±0.09	10.08±0.08	10.12±0.07
Glucose(mg/dl)	1	87.04±4.14	91.95±6.57	100.44±6.87**	103.45±6.44**	105.2±4.72**	89.8±3.45	89.23±3.57	88.13±3.74
	2	85.31±2.32	87.04±2.68	88.9±2.88**	91.44±3.14**	98.56±2.1**	86.52±2.09	85.76±2.37	85.59±2.49
Total Protein(g/dl)	1	6.20±0.26	6.02±0.27	5.82±0.28*	5.75±0.25*	5.89±0.29	6.05±0.28	6.13±0.28	6.19±0.28
	2	6.01±0.19	5.87±0.22	5.77±0.28*	5.74±0.27*	5.86±0.26	5.89±0.24	5.90±0.25	5.93±0.23
Blood urea nitrogen(mg/dl)	1	20.5±0.67	21.2±0.56	21.54±0.66**	21.71±0.65**	21.32±0.62**	20.7±0.68	20.66±0.68	20.64±0.64
	2	21.24±0.62	21.78±0.51	22.12±0.5**	22.3±0.59**	22.05±0.77**	21.55±0.7	21.51±0.69	21.32±0.66
Creatinine(mg/dl)	1	0.91±0.08	0.97±0.06	1.07±0.09**	1.12±0.1**	1.03±0.09	0.96±0.03	0.89±0.04	0.89±0.04
	2	1.02±0.04	1.07±0.04	1.14±0.05*	1.16±0.05*	1.08±0.04	1.06±0.03	1.04±0.03	1.03±0.03
Sodium(mEq/dl)	1	140.09±0.95	140.24±0.98	140.45±1.03*	140.57±1.01*	140.50±1.04*	140.34±1.01*	140.15±0.96	140.15±1.07
	2	138.61±21.89	138.65±0.63	139.58±0.69*	139.82±0.7*	138.81±0.7*	138.7±0.69*	138.61±0.67	138.58±0.64*
Potassium(mEq/dl)	1	4.40±0.16	4.30±0.12	4.25±0.13*	4.19±0.16*	4.22±0.18	4.31±0.12	4.37±0.14	4.39±0.16
	2	4.05±0.06	3.97±0.06	3.70±0.10**	3.55±0.08**	3.87±0.07	3.95±0.08	4.02±0.07	4.04±0.07
Chloride(mEq/dl)	1	103.35±1.53	103.07±1.48	102.89±1.49**	102.76±1.48**	102.91±1.49*	103.06±1.48	103.25±1.51	103.33±1.53
	2	107.99±1.86	107.78±1.89	106.76±1.78**	106.52±1.79**	107.74±1.89	108.01±1.96	108.19±1.89	108.14±1.89
AST (IU/L)	1	29.58±1.13	30.14 2.65**	30.38 2.73**	30.36 2.8*	30.3 1.51*	30.06 1.57*	29.8 2.89	29.73 2.74
	2	24.85± 0.39	25.19± 0.48*	25.27± 0.46**	25.27± 0.41	24.96± 0.38	24.91± 0.44	24.88± 0.14	24.87± 0.4
ALT(IU/L)	1	29.59± 0.58	29.97± 0.56	30.5± 0.67**	30.88± 1.91**	30.31± 0.72*	29.81± 0.61	29.58± 0.58	29.65± 0.63
	2	30.24± 0.8	30.54± 0.79	30.62± 0.81**	30.87± 0.86**	30.39 ± 0.85	30.37± 0.85	30.36± 0.76	30.26± 0.79

* Significant at $p<0.05$ difference with 0 min time interval

** Significant at $p<0.01$ difference with 0 min time interval

References

1. Abou-Ghanema II, El-Kammar MH, El-Khamary AN. Anaesthetic effects, chemical restraint, clincophysiological and haematobiochemical findings after intravenous, detomidine/ ketamine/ midazolam combination in Buffalo Calves. Global Veterinaria, 12 2014; (3):351-360.
2. Aguado D, Benito J, Gomez D, Segura IA. Reduction of the minimum alveolar concentration of isoflurane in dogs using a constant rate of infusion of lidocaine-ketamine in combination with either morphine or fentanyl. Vet. J 2011; 189:63-66.
3. Ahmad RA, Amarpal Kinjavdekar P, Aithal HP, Pawde AM, Kumar D. Potential use of dexmedetomidine for different levels of sedation, analg. and anaesth. in dogs. Vet Med. 2013; 58(2):87-95.
4. Amarpal Santosh KM, Ahmad RA, Kinjavdekar P, Aithal HP, Pawde AM, Kumar D. Evaluation of midazolam-ketamine with dexmedetomidine and fentanyl for injectable anaesthesia in dogs. Veterinarski Archiv. 2013; 83(5):509-523.
5. Ambrisko TD, Hikasa Y. Neurohormonal and metabolic effect of Medetomidine compared with Xylazine in beagle dogs. Can. J Vet. Res. 2002; 64:42-49.
6. Barletta M, Austin BR, Ko JC, Payton ME, Weil AB, Inoue T. Evaluation of dexmedetomidine and ketamine in combination with opioids as injectable anesthesia for castration in dogs. J Am. Vet. Med. Assoc. 2011; 238:1159-1167.
7. Bayan H, Konwar B. Clinical evaluation of ketamine-propofol anaesthesia in dog. Indian J of Field Veterinarians. 2014; 10(2):41-42.
8. Church DB, Nicholson AI, Ilkiw JE, Emslie DR. Effect of non-adrenal illness, anaesthesia and surgery on plasma cortisol concentrations in dogs. Res. Vet. Sci. 1994; 56(1):129-131.
9. Dollery SC. Therapeutic Drugs. Churchill Livingstone, London, A. 1991, 21.
10. Felsner P, Hofer D, Rinner I, Porta S, Korsatko W, Schauenstein K. Adrenergic suppression of peripheral blood T cell reactivity in the rat due to activation of α-2-receptors. J Neuroimmunol. 1995; 57:27-34.
11. Gerlach AT, Dasta JF, Steinberg S, Martin LC, Cook CH. A new dosing protocol reduces dexmedetomidine-associated hypotension in critically ill surgical patients. J of Crit. Care. 2009; 24:568-574.
12. Gill AG. Decrease in plasma potassium in rabbit. J Am. Assoc. Lab Anim. Sci. 2004; 49(1):52-56.
13. Granholm M, McKusick BC, Westerholm FC, Aspergen JC. Evaluation of the clinical efficacy and safety of IM and IV doses of dexmedetomidine and medetomidine in dogs and their reversal with atipamazole. Vet. Rec. 2007; 160:891-897.
14. Haskins SC, Farver TB, Patz JD. Ketamine in dogs. Am. J Vet. Res. 1985; 46(9):1855-1860.
15. Jadon NS, Kumar A, Sharma B, Singh SP. Detomidine as a preanaesthetic in thiopentone anaesthesia in dogs. Indian J Anim. Sci. 1998; 68:48-49.
16. Joubert KE, Lobetti R. The cardiovascular and respiratory effect of medetomidine and thiopental anesthesia in dogs breathing at an altitude of 1486m. J. S. Afr. Vet. Assoc. 2002; 73(3):104-10.

17. Kim JW, Jang IH. The effect of xylazine. premedication on propofol anaesthesia in the dog. Kor. J Vet. Clin. Med. 1999; 16:86-94
18. Koichev K, Golemanov D, Houbenov H, Aminokov B. Experimental study on effect of 'domosedan' in sheep and cattle. J Assoc. Vet. Anaes. 1988; 15:114.
19. Lemke KA. Anticholinergics and sedatives. Lumb and Jones' Veterinary Anesthesia and Analgesia. 4th ed. Tranquilli, W.J., Thurmon, J.C., Grimm, K.A., eds. Ames, IA: Blackwell. 2007, 203-239.
20. Leppanen MK, Mc Kusick BC, Granholm MM, Westerholm FC, Tulamo R, Short CE. Clinical efficacy and safety of dexmedtomidine and buprenorphine, bitorphaanol or diazepam for canine hip radiography. J Small Anim. Prac. 2006; 47:663-669.
21. Lerche P, Muir W. Effect of medetomodine on breathing and inspiratory neuromuscular drive in conscious dogs. Am. J Vet. 2004; 65:720-24.
22. Lerche P, Reid J, Nolan AM. Comparative study of propofol or propofol and ketamine for the induction of anaesthesia in dogs. J of the British Vet. Assoc. 2000; 146(20).
23. Lyon Lee. pharmacology - intravenous anesthetic agents & dissociatives. Vet. Surg. 2000; 1:1-14.
24. Mazumdar H, Sarma B, Sarma KK, Mazumdar A. Haematological and biochemical effect of dexmedetomidine in dogs. IJRSR. 2015; 6(7):5301-5303.
25. McCarthy DA, Chen G. General anaesthetic action of 2-(O chlorophenyl) -2 methylamino-cyclohexanone HCL (CI-581) in rhesus monkey (Abstract 76 a). Fed. Proc. 1965; 24:268.
26. Posner LP, Burns P. Injectable anesthetics. In: Riviere JE, Papich MG (eds.), Veterinary Pharmacology and Therapeutics. 9th edn., John Wiley and Sons, USA. 2009, 279-284.
27. Sabbe MB, Penning JP, Ozaki GT. Spinal and Systemic action of the α-2 receptor agonist Dexmedetomidine in dogs. Antinociception and carbon dioxide response. Anaesthesiology. 1994; 80(5):1057-72.
28. Sadik Y, Nadide K, Alkan K. Comparision of Intravenous and Intraosseous Administration of Propofol-Ketamine Combination for Anesthesia in Quails (*Coturnixcoturnix japonica*). Kocatepe Vet J. 2012; 7(1):11-16.
29. Sarzan RD, Starke WA, Krause GF, Garner HE. Cardiovascular effect of Detomidine, a new alpha-2 agonist in the conscious pony. J Vet. Pharmacol. Ther. 1989; 12:378-388.
30. Schalm OW, Jaim NC, Carrel EJ. Veterinary Haematology. 3rd edn., Lea and Febigar, Philadelphia, 1975, 258-276.
31. Sindak N, Camkerten I, Ceylan C. Clinical evaluation of ketamine –xylazine anaesthesia in bozova greyhounds. J of Anim and Vet. Advance. 2010; 9(15):2025-2029.
32. Skarda RT, Muir WW. Comparison of antinociceptive, cardiovascular and respiratory effects, head ptosis and position of pelvic limbs in mares after caudal epidural administration of xylazine and detomidine hydrochloride solution. Am. J Vet. Res. 1996; 51:556-560.
33. Smith G, Tharburn J, Vance JP, Brown DM. The effect of ketamine on the canine coronary circulation. Anaesthesiology. 1979; 34:555.
34. Snedecor GW, Cochran SE. Statistical methods.6th ed. Iowa State University Press, Iowa, U.S.A. 1980.
35. Stevenson DE. A decrease in plasma potassium concentration was observed during anaesthesia without any significant change in plasma sodium concentration. Brit. Vet J. 1960; 119:477-83.
36. Surbhi, Kinjavdekar P, Amarpal, Aithal HP, Pawde AM, Pathak MC *et al*. Physiological and biochemical effects of medetomidine- butorphanol, propofol anaesthesia in dogs undergoing orthopaedic surgery. Indian. J Vet. Surg. 2010; 31:101-104.
37. Umar MA, Adam MK. Effects of Combination of Ketamine-Medetomidine Anaesthesia on Haematology and Some Serum Chemistry Parameters in Dogs. J home. 2013; 34(3):808-813
38. Venn R, Hell J, Grounds RM. Respiratory effects of dexmedetomidine in the surgical patient requiring intensive care. Crit. Care. 2000; 4:302-8.
39. White PF, Way WL, Trevor AJ. Ketamine, its pharmacology and therapeutic uses. Anesthesiology. 1982; 56:119-136.
40. Wilson J, Doherty TJ, Egger CM, Fidler A, Cox S, Rohrbach B. Effects of intravenous lidocaine, ketamine, and the combination on the minimum alveolar concentration of sevoflurane in dogs. Vet. Anaesth. Analg. 2008; 35:289-296