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Haemato-biochemical alterations following administration of butorphanol, dexmedetomidine and acepromazine as premedicants in combination with thiopentone sodium for inducing general anaesthesia in canines

Bhanu Brijlal Khutey, Raju Sharda, Rukmani Dewangan, SK Tiwari, Sumeet Pal and MV Kamble

Abstract
The present study was conducted on 18 healthy dogs of either sex weighing between 10-20 kg to evaluate the alternations on haemato-biochemical parameters following administration of butorphanol, dexmedetomidine and acepromazine as premedicants in combination with thiopentone sodium for inducing general anaesthesia. The experimental work was divided into three groups BT (butorphanol-thiopentone sodium), DT (dexmedetomidine-thiopentone sodium) and AT (acepromazine-thiopentone sodium). Glycopyrrolate @ 0.02 mg/ kg intramuscularly was administered 10 minutes prior to treatment in all the groups of animals. The animals of group BT, DT and AT were premedicated intramuscularly with butorphanol @ 0.3 mg/kg b.wt. Dexmedetomidine @ 10 µg/kg b.wt. And acepromazine @ 0.4 mg/kg b.wt. Respectively and general anaesthesia was induced with thiopentone @ 18 mg/kg b.wt. Intravenously. Haematological parameters *viz.* Hb, PCV, TEC, TLC and DLC and biochemical parameters *viz.* serum glucose, serum total protein, serum urea nitrogen, serum creatinine, ALT and AST were estimated before sedation (0) and at 30, 60,120 min. and 6 hrs post thiopentone anaesthesia. Haematological studies revealed non-significant changes in haemoglobin, packed cell volume, total erythrocyte count and total leucocyte count following thiopentone anaesthesia at various time intervals in all the groups. There was significant ($p<0.05$) increase in neutrophils with a consequent non-significant decrease in lymphocyte values in all the three groups. Serum glucose showed a significant ($P<0.01$) increase in all the groups initially which returned to base values by 6 hrs. Other biochemical parameters like serum total protein, serum urea nitrogen, serum creatinine and serum enzymes *viz.* AST and ALT values showed non-significant changes at various time intervals in all the three groups but were within normal range. It was concluded that thiopentone sodium in combination with butorphanol, dexmedetomidine and acepromazine does not produce any harmful effect on vital organs and changes remained within physiological limits, thus combinations can be safely used as a general anaesthetic in canines.

Keywords: Acepromazine, biochemical, butorphanol, canines, dexmedetomidine, glycopyrrolate, haematological, premedicants, thiopentone sodium

Introduction
Anaesthesia is an integral part of veterinary surgery and a successful surgery can only be performed under safe anaesthesia. Depending upon the requirement in clinical practice and convenience, anaesthetic drugs with different protocols have been evolved through steady flow of research. An ideal anaesthetic agent should provide good muscle relaxation, adequate analgesia, sedation along with smooth induction and safe recovery. No single anaesthetic drug produces all of the components of general anaesthesia without depressing some vital organ function. Therefore, in veterinary anaesthesia combinations of sedatives, tranquilizers, analgesics and general anaesthetics have been widely used in animal practice to attain desirable effect of general anaesthesia. The uses of premedicant have been reported for safe and smooth induction of anaesthesia along with sparing effect on the induction dose of intravenous anaesthetics.
Glycopyrrolate is a synthetic quaternary ammonium compound, anticholinergic with no central effects. It has a powerful and prolonged anti sialagogue activity and is about five times as potent as atropine (Hall *et al.*, 2001) [6].

It blocks peripheral muscarinic receptors, thus inhibiting cholinergic transmission. Opioid analgesic is used primarily to produce analgesia without resulting in loss of consciousness. These are included in balanced anaesthesia protocols for their analgesic effect, but also have sedative effect. Butorphanol is a central-acting analgesic with both narcotic agonist and antagonist properties like μ-receptor antagonist and κ-receptor agonist. It is a morphine derivative, which is a synthetic analgesic and 3 to 5 times more potent than morphine (Pircio *et al.*, 1976) [13]. Dexmedetomidine is an alpha-2 adrenergic receptor agonist used for sedation, analgesia and also as an adjunct to anesthesia for reducing anesthetic requirements in procedures requiring total intravenous anesthesia (Miller, 2009) [12]. The onset of action is 5 and 10-15 minutes after intravenous and intramuscular administration, respectively. The most common side effects of dexmedetomidine are bradycardia, decreased respiration and hypothermia. Acepromazine is a phenothiazine tranquilizer that blocks dopamine receptors in the CNS and depresses the reticular activating system resulting in sedation. It is metabolized by the liver and eliminated by the kidney and as a result has longer half-life in young animals. It produces 4-8 hours effect in neonates and juveniles. It also possesses antiemetic, antihistaminic, antiarrhythmic and antishock properties because of its dopamine inhibition in the chemoreceptor trigger zone (Turi and William 2011) [20]. Thiopentone sodium is an ultra-short acting barbiturate that has been used in various species of animals to produce a short term surgical anaeshesia. Thiopental sodium is a powerful hypnotic that produces dose-dependent depression of the central nervous system (Jodon *et al.*, 1998) [7]. Rapid intravenous injection cause fall in blood pressure as a result of direct depressant effect on myocardium. The therapeutic dose of barbiturate depresses respiration. Therefore, the purpose of this study was to evaluate the alternations on haemato-biochemical parameters following administration of butorphanol, dexmedetomidine and acepromazine as premedicants in combination with thiopentone sodium for inducing general anaesthesia.

Materials and methods

The present study was conducted on 18 healthy dogs of either sex weighing between 10 to 20 kg body weight and were randomly divided into three groups *viz*., group BT, group DT and group AT, comprising of 6 animals in each. The animals were fasted overnight and drinking water was withheld for 4 hours before the administration of anaesthesia. Ten minutes prior to the anaesthetic administration, all dogs were administered glycopyrrolate @ 0.02 mg/kg b.wt. Intramuscularly. The animals of group BT, DT and AT were premedicated intramuscularly with butorphanol @ 0.3 mg/kg b.wt. Dexmedetomidine @ 10 µg/kg b.wt. And acepromazine @ 0.4 mg/kg b.wt. Respectively. After premedication, general anaesthesia was induced by thiopentone @ 18 mg/kg b.wt. Intravenously in all the groups and dogs were intubated by suitable endotracheal tube of (4.5 to 8.5 OD mm) with guidance of laryngoscope. The venous blood samples were taken before induction, 30, 60 120 min. and 6 hr. in vial with EDTA and without EDTA from the recurrent tarsal vein to estimate alteration in various haemato-bichemical parameters using semi-automatic haematological analyzer (HDC 5-Part MS4S2) and semi-automatic biochemical analyzer (ERBA Chem 7). The haematological parameters estimated were haemoglobin (Hb), packed cell volume (PCV), total erythrocyte count (TEC), total leucocyte count (TLC), differential leucocyte count (DLC) and biochemical parameters *viz*., serum glucose, serum total protein, serum urea nitrogen (SUN), serum creatinine, alanine amino transferase (ALT) and aspartate amino transferase (AST). Analysis of variance (ANOVA) and Duncan's multiple range tests (DMRT) were applied to compare mean within group and between groups using SPSS v25 statistics software program and data was presented as Mean±S.E. Statistically significant differences were considered at 5 percent level (5%).

Results and Discussion

Haematological Parameters

A) Haemoglobin (Hb)

In the animals of group DT following dexmedetomidine-thiopentone anaesthesia, mean haemoglobin value decreased non-significantly up to 120 minutes interval (12.02±0.20 to 11.17±0.83 g/dl) where as in animals of group BT (Butorphanol + thiopentone sodium) and group AT (Acepromazine + thiopentone sodium) a non-significant decrease in haemoglobin was observed upto 60 minutes (11.83±0.67 to 11.23±0.67 g/dl) and (11.46±0.67 to 10.99±0.06 g/dl) respectively (Table 1). However, the values in all the three groups returned to near pre administration values by the end of study period. The decrease in haemoglobin level in animals of all the three groups could be due to the pooling of erythrocytes in spleen or other reservoirs induced by adrenolytic property of alpha-2 agonist as also observed with most of the anaesthetics (Lim *et al*., 2000; Bayan *et al*., 2002) [10, 1] in dogs. It might also be attributed to haemodilution in response to fluid therapy (Skarda and Muir, 1996) [17]. A similar decrease in the haemoglobin was also recorded during thiopentone anaesthesia in dogs (Saini *et al*., 2017; Fulsunge *et al*., 2019) [14, 5]. However, the values of haemoglobin differed none significantly between the three groups.

Table 1: Showing effect of various anaesthetic protocol on haemoglobin (g/dL) in different groups at various time intervals (Mean ± SE)

Parameter	Groups (n=6)	Post -Anaesthesia (Min.)				
		0	30	60	120	6Hrs
Hb (g/dL)	A	11.83±0.67^{Aa}	11.48±0.83^{Aab}	11.23±0.67^{Aab}	11.34±0.33^{Aab}	11.78±0.33^{Aa}
	B	12.02±0.20^{Aa}	11.64±0.33^{Aab}	11.46±0.83^{Aab}	11.17±0.83^{Aab}	11.93±0.33^{Aa}
	C	11.46±0.67^{Aa}	11.14±0.83^{Aab}	10.99±0.06^{Aab}	11.06±0.03^{Aa}	11.35±0.50^{Aa}

ABC-Values bearing different superscript vary significantly (P<0.05) between groups
abc- Values bearing different superscript vary significantly (P<0.05) within groups

B) Packed Cell Volume

A non-significant decrease in PCV values from 39.05±0.10 to 37.71±0.83%; 39.68±0.50 to 36.79±0.10% and 36.38±0.57 to 32.61±0.67% in Group BT, DT and AT respectively was observed up to 60 minutes interval (Table 2). Subsequently, a gradual increase in the level of PCV was noted from 120

minutes onwards till the completion of observation. However, the values returned to the base level between 2 to 6hrs in animals of all the groups. The decrease in PCV can be expected due to pooling of circulating erythrocytes in the spleen and other reservoirs secondary to decreased sympathetic stimulation as also reported by (Skarda and Muir, 1996) [17] after administration of tranquilizers in dogs. The marginal reduction in PCV during the entire period of anaesthesia or sedation in animals of three groups might also be due to shifting of fluid from extravascular compartment to intravascular compartments on account of vasodilatation resulting in vascular pooling in order to maintain normal cardiac output in the animals (Wagner *et al*., 1991) [20]. Similar finding have also been observed following administration of alpha-2 adrenergic agonist along with barbiturate drug in dogs (Saini *et al*., 2019) [15].

Table 2: Showing effect of various anaesthetic protocol on packed cell volume (%) in different groups at various time intervals in dogs (Mean ± SE).

Parameter	Groups (n=6)	Post -Anaesthesia (Min.)				
		0	30	60	120	6 Hrs
PCV (%)	A	39.05±0.10^{Aa}	38.34±0.67^{Aa}	37.71±0.83^{Ab}	38.01±0.50^{Aa}	39.01±0.33^{Aa}
	B	39.68±0.50^{Aa}	38.03±0.33^{Aa}	36.79±0.10^{Aab}	37.61±0.33^{Aa}	39.93±0.50^{Aa}
	C	36.38±0.57^{Aa}	34.23±0.69^{Aa}	32.61±0.67^{Ab}	33.45±0.25^{Aa}	36.05±0.02^{Aa}

ABC-Values bearing different superscript vary significantly (P<0.05) between groups
abc- Values bearing different superscript vary significantly (P<0.05) within groups

C) Total Erythrocyte Count

There was a non-significant decrease in total erythrocyte count in the animals anaesthetized with dexmedetomidine + thiopentone sodium (Group DT) up to 120 minutes interval (5.92±0.19 to 4.47±0.50 x10^6 /µL). On the other hand, the decrease in TEC persisted up to 60 minutes (6.37±0.17 to 5.76±0.67 x10^6 /µL) and (6.08±0.06 to 5.30±0.33 x10^6 /µL) in animals which were administered a combination of butorphanol + thiopentone sodium (Group BT) and acepromzine + thiopentone sodium (Group AT) anaesthesia respectively (Table 3). A comparatively increased period of erythrocytopenia was observed with alpha-2 agonist drug and barbiturate could be due to more potent cardiopulmonary depression. However, the transitional alterations returned to the pre administration levels by 6 hours of study period. A non-significant decrease in TEC might also be due to spleenic pooling of red blood cells during early stage of anaesthesia. Similar observations were also reported following administration of alpha-2 agonist along with thiopentone sodium in dogs. (Jadon *et al.*, 1998) [7].

Table 3: Showing effect of various anaesthetic protocol on total erythrocytes (x 10^6 /µL) in different groups at various time intervals in dogs (Mean ± SE).

Parameter	Groups	Post -Anaesthesia (Min.)				
		0	30	60	120	6Hrs
TEC (x 106 /µL)	A	6.37±0.17Aa	6.08±0.17Ab	5.76±0.67Aa	6.00±0.83Aa	6.33±0.50Aa
	B	5.92±0.19Aa	4.89±0.33Aa	4.70±0.83Aab	4.47±0.50Aa	5.89±0.17Aa
	C	6.08±0.06Aa	5.34±0.17Aa	5.30±0.33Aa	5.42±0.17Aa	5.92±0.26Aa

ABC-Values bearing different superscript vary significantly (P<0.05) between groups
Abc- Values bearing different superscript vary significantly (P<0.05) within groups

D) Total Leucocyte Count

In the animals of group DT, following thiopentone anaesthesia the mean total leucocyte count decreased non-significantly (10.12±0.08 to 9.31±0.67 ×10^3/µL) up to 120 minutes interval where as in animals of group BT and AT, a non-significant decrease in total leucocyte count was observed upto 60 minutes interval from 11.04±0.33 to 10.27±0.19 ×10^3/µL and 10.40±0.83 to 9.93±0.31 ×10^3/µL respectively (Table 4). However, the values in all the three groups returned to near preadministration by the end of study period. The decrease in total leucocyte count in animals of all the three groups could be due to the pooling of erythrocytes in spleen or other reservoirs induced by adrenolytic property of alpha-2 agonist as also observed with most of the anaesthetics (Lim *et al*., 2000; Bayan *et al*., 2002) [10, 1] in dogs. It might also be attributed to haemodilution in response to fluid therapy (Skarda and Muir, 1996) [17]. A decrease in leucocyte values was also recorded during thiopentone anaesthesia in dogs (Saini *et al*., 2017; Fulsunge *et al*., 2019) [14, 5]. However, the values of haemoglobin differed non-significantly between the three groups.

Table 4: Showing effect of various anaesthetic protocol on total leucocyte count (×10^3/µL) in different groups at various time intervals in dogs (Mean ± SE)

Parameter	Groups (n=6)	Post -Anaesthesia (Min.)				
		0	30	60	120	6Hrs
TLC (×10^3 / µL)	A	11.04±0.33^{Aa}	10.65±0.67^{Aa}	10.27±0.19^{Aa}	10.72±0.83^{Aa}	11.02±0.33^{Aa}
	B	10.12±0.08^{Aa}	9.75±0.10^{Aa}	9.69±0.37^{Aa}	9.31±0.67^{Aa}	10.05±0.83^{Aa}
	C	10.40±0.83^{Aa}	10.21±0.04^{Aa}	9.93±0.31^{Aa}	10.12±0.33^{Aa}	10.41±0.67^{Aa}

ABC- Values bearing different superscript vary significantly (P<0.05) between groups
abc- Values bearing different superscript vary significantly (P<0.05) within groups

E) Neutrophils (%)

In the animals of group DT following dexmedetomidine-thiopentone anaesthesia the mean neutrophils count increased non-significantly from 60.18±0.83 to 62.93±0.69% upto 120 minutes interval where as in animals of group BT (butorphanol + thiopentone sodium) and group AT

(acepromazine + thiopentone sodium) a non-significant increase in neutrophils count was observed from 65.73±0.33 to 66.68±0.33% and 65.18±0.50 to 65.79±0.67% upto 60 minutes respectively (Table 5). However, the values in all the three groups returned to near pre administration by the end of study period. The insignificant fluctuating changes in differential leucocyte count may be due to stress and release of ACTH (Felser *et al*., 1995). A similar observation was also reported with dexmedetomidine and thiopental sodium anaesthesia in dogs (Saini *et al*., 2019) [15].The rise in neutrophil count might also be attributed to the adrenocortical stimulation and subsequent effect of glucocorticoids on circulating neutrophils (Soliman *et al*., 1965) [18].

Table 5: Showing effect of various anaesthetic protocol on Neutrophil Count (%) in different groups at various time intervals (Mean ± SE)

Parameter	Groups (n=6)	Post -Anaesthesia (Min.)				
		0	30	60	120	6hr
Neutrophils (%)	A	65.73±0.33^{Aa}	66.20±0.17^{Aa}	66.68±0.33^{Aa}	66.41±0.67^{Aa}	65.78±0.33^{Aa}
	B	60.18±0.83^{Aa}	62.51±0.09^{Aa}	62.70±0.00^{Aa}	62.93±0.69^{Aa}	60.14±0.39^{Aa}
	C	65.18±0.50^{Aa}	65.55±0.33^{Aa}	65.79±0.67^{Aa}	65.45±0.20^{Aa}	65.10±0.83^{Aa}

ABC-Values bearing different superscript vary significantly (P<0.05) between groups
abc- Values bearing different superscript vary significantly (P<0.05) within groups

F) Lymphocytes (%)

There was a non-significant decrease in lymphocyte count in Group DT from 32.85±0.17 to 29.37±0.83% upto 120 minutes in the animals which were anaesthetized with dexmedetomidine and thiopentone sodium anaesthesia. On the other hand, the decrease in lymphocyte value persisted up to 60 minutes from 29.06±0.67 to 28.46±0.33% and 29.23±0.50 to 28.74±0.08% in animals of Group BT and Group AT respectively (Table 6). A comparatively prolonged period of lymphocytopaenia observed with Alpha-2 agonist drug and barbiturate could be due the adrenocortical stimulation and subsequent effect of glucocorticoids on circulating lymphocytes (Soliman *et al*., 1965) [18]. However, the marginal changes returned to the pre administration levels by 6 hours of study period. There was a corresponding lymphocytopaenia in response to neutrophilia in all the group of animals after various anaesthetic regimen.The non-significant decrease in differential leucocyte count observed in this study, could have resulted due to stress and release of ACTH, on account of anaesthetic drug administration (Felsner *et al*., 1995) [4]. Similarly reduced levels of lymphocytes were also recorded under thiopentone- medetomidine anaesthesia in dogs (Saini *et al*., 2019) [15].

Table 6: Showing effect of various anaesthetic protocol on Lymphocyte Count (%) in different groups at various time intervals in dogs (Mean ± SE**)**

Parameter	Groups (n=6)	Post -Anaesthesia (Min.)				
		0	30	60	120	6hr
Lymphocytes (%)	A	29.06±0.67^{Aa}	28.84±0.83^{Aa}	28.46±0.33^{Aa}	28.96±0.67^{Aa}	29.01±0.33^{Aa}
	B	32.85±0.17^{Aa}	30.57±0.17^{Aa}	29.83±0.83^{Aa}	29.37±0.83^{Aa}	32.77±0.50^{Aa}
	C	29.23±0.50^{Aa}	29.08±0.33^{Aa}	28.74±0.08^{Aa}	28.89±0.33^{Aa}	29.22±0.20^{Aa}

ABC-Values bearing different superscript vary significantly (P<0.05) between groups
abc- Values bearing different superscript vary significantly (P<0.05) within groups

G) Monocytes (%)

In the animals of DT following dexmedetomidine-thiopentone anaesthesia, the mean monocyte count decreased non-significantly from 4.20±0.50 to 3.15±0.12% up to 120 minutes interval where as in animals of group BT and group AT, a non-significant decrease in monocyte count was observed upto 60 minutes from 2.86±0.61 to 2.33±0.23% and 2.38±0.67 to 1.94±0.10% respectively (Table 7). However, the values in all the three groups returned to near pre administration by the end of study period. The values of monocyte did not showed any significant changes within and between the groups.

Table 7: Showing effect of various anaesthetic protocol on monocyte count (%) in different groups at various time intervals. (Mean ± SE)

Parameter	Groups (n=6)	Post -Anaesthesia (Min.)				
		0	30	60	120	6hr
Monocyte (%)	A	2.86±0.61^{Aa}	2.75±0.10^{Aa}	2.33±0.23^{Aa}	2.45±0.40^{Aa}	2.84±0.38^{Aa}
	B	4.20±0.50^{Aa}	3.61±0.42^{Aa}	3.43±0.33^{Aa}	3.15±0.12^{Ba}	4.18±0.63^{Aa}
	C	2.38±0.67^{Aa}	2.09±0.17^{Aa}	1.94±0.10^{Aa}	2.29±0.07^{Aa}	2.38±0.50^{Aa}

ABC-Values bearing different superscript vary significantly (P<0.05) between groups
abc- Values bearing different superscript vary significantly (P<0.05) within groups

H) Eosinophils (%)

After administration of dexmedetomidine and thiopentone sodium anaesthesia in the animals of group DT, the mean eosinophil count decreased non-significantly from 2.39±0.23 to 1.91±0.83% up to 120 minutes interval where as in animals of group BT (butorphanol + thiopentone sodium) and group AT (acepromazine + thiopentone sodium) a non-significant decrease in eosinophil count was observed from 2.03±0.33 to 1.58±0.53% and 2.85±0.17 to 2.08±0.50% upto 60 minutes respectively (Table 8). However, the values in all the three groups returned to near pre administration by the end of study period. Eosinophils showed a non-significant decrease in all the groups of animals after drug administration. This possibly might be attributed to the adrenocortical stimulation and subsequent effect of glucocorticoids (Soliman *et al.*, 1965) [18]. The value of eosinophils did not show any significant changes within and between the groups.

Table 8: Showing effect of various anaesthetic protocol on eosinophil count (%) in different groups at various time intervals. (Mean ± SE)

Parameter	Groups (n=6)	Post -Anaesthesia (Min.)				
		0	30	60	120	6hr
Eosinophils (%)	A	2.03±0.33^{Aa}	1.93±0.43^{Aa}	1.58±0.53^{Aa}	1.90±0.05^{Aa}	2.04±0.17^{Aa}
	B	2.39±0.23^{Aa}	2.23±0.50^{Aa}	2.02±0.83^{Ba}	1.91±0.83^{Aa}	2.38±0.57^{Aa}
	C	2.85±0.17^{Aa}	2.52±0.56^{Aa}	2.08±0.50^{Aa}	2.28±0.30^{Aa}	2.83±0.50^{Aa}

ABC-Values bearing different superscript vary significantly (P<0.05) between groups
abc- Values bearing different superscript vary significantly (P<0.05) within groups

Biochemical Parameters

(a) Glucose

Serum glucose levels increased in all the groups after administration of thiopentone anaesthetic drug. There was significant (P<0.05) increase in serum glucose level in animals of group BT from 82.24±0.04 to 94.07±0.32 mg/dL up to 60 min post anaesthesia with the highest value at 60 min. (94.07±0.32). In group DT, a significant (P<0.05) increase in serum glucose was recorded from 84.57±0.83 to 101.92±0.17 mg/dL upto 120 min. interval which was followed by gradual decrease in serum glucose up to 6 hrs. Animals of group AT also showed a significant (P<0.05) increase in serum glucose values from 82.17±0.83 to 94.96±0.67 mg/dL at 60 min. interval (Table 9). Thereafter, the values decreased and returned to normalcy by 6 hrs. In all the three groups. The rise in serum glucose level in all the groups might be attributed to the effect of alpha-2 adrenoceptor agonists that was associated with growth hormone stimulation and insulin suppression through direct inhibitory effect of dexmedetomidine on the pancreatic beta-cells (Dollery, 1991) [3]. Thevalues have similarity with the findings of Saini *et al.* (2017) [14] and Shaaban *et al*. (2018) [16]. Jadon *et al.*, (1998) [7] who reported increased level of glucose in dogs subjected to detomidine and thiopental sodium anaesthesia. The rise in glucose values might be due to an increase in circulatory catecholamines after premedication (Hall *et al.*, 1994) and also the effect of the anaesthetic agent on a subcortical pathway, which might be responsible for the regulation of adrenocorticotropic hormone (ACTH) producing stress like conditions with increased release of glucocorticoids.

Table 9: Showing effect of various anaesthetic protocol on serum glucose (mg/dL) in different groups at various time intervals. (Mean ± SE)

Parameter	Groups (n=6)	Post -Anaesthesia (Min.)				
		0	30	60	120	6hr
Serum Glucose (mg/dL)	A	82.24±0.04^{Aa}	88.98±0.03^{Ab}	94.07±0.32^{Ac}	86.92±0.67^{Ab}	81.55±0.35^{Aa}
	B	84.57±0.53^{Aa}	90.45±0.43^{Ab}	95.74±0.33^{Ac}	101.92±0.27^{Abc}	85.78±0.50^{Aa}
	C	82.17±0.83^{Aa}	89.24±0.17^{Ab}	94.96±0.67^{Ac}	88.76±0.67^{Ab}	81.37±0.02^{Aa}

ABC-Values bearing different superscript vary significantly (P<0.05) between groups.
abc- Values bearing different superscript vary significantly (P<0.05) within groups.

(b) Serum Total Protein

In animals as group BT, a non-significant decrease in serum protein was reported up to 60 min. from 6.56±0.67 to 6.12±0.53 g/dl after administration of butorphanol-thiopentone sodium. Later on, the values returned to normalcy between 5- 6 hrs. In group DT, a non-significant decrease was recorded up to 60 min. from 7.71±0.17 to 7.13±0.67 g/dL after administration of dexmedetomidine-thiopentone sodium anaesthesia which gradually returned to near preadministration level by 6 hrs. In group AT, a non-significant decrease was reported up to 60 min. from 7.54±0.03 to 6.92±0.83 g/dL after administration of acepromazine-thiopentone sodium (Table 10). Later on, the values returned to normalcy by the end of the study period. This non-significant decrease in total serum protein after alpha-2 agonist and thiopental sodium administration observed in this study might be due to haemodilution or may be inter compartmental fluid shift causing haemodilution (Saini *et al*., 2017) [14]. Jadon *et al*., (1998) [7] have also reported decrease in total protein levels in dogs after administration of detomidine and thiopentone sodium anaesthesia.

Table 10: Showing effect of various anaesthetic protocol on serum glucose (mg/dL) in different groups at various time intervals in. (Mean ± SE)

Parameter	Groups (n=6)	Post-Anaesthesia (Min.)				
		0	30	60	120	6hr
Serum Total protein	A	6.56±0.67^{Aa}	6.19±0.07^{Aa}	6.12±0.53^{Aa}	6.23±0.03^{Aa}	6.29±0.33^{Aa}
	B	7.71±0.17^{Aa}	7.44±0.13^{Aa}	7.23±0.05^{Aa}	7.13±0.67^{Aa}	7.56±0.04^{Aa}
	C	7.54±0.03^{Aa}	7.16±0.67^{Aa}	6.92±0.83^{Aa}	7.25±0.47^{Aa}	7.41±0.50^{Aa}

ABC-Values bearing different superscript vary significantly (P<0.05) between groups
abcdf- Values bearing different superscript vary significantly (P<0.05) within groups

(c) Serum Urea Nitrogen

In animals of group DT, the mean serum urea nitrogen value increased non- significantly from 21.61±0.67 to 22.32±0.33 mg/dL up to 120 minutes interval where as in animals of group BT and AT, a non-significant increase in serum urea nitrogen value upto 60 minutes was observed from 20.72±0.50 to 21.03±0.33 mg/dL and 21.03±0.83 to 21.47±0.32 mg/dL respectively (Table 11). However, the values in all the three groups returned to near pre administration by the end of study period. The increase in SUN level after anaesthesia in all the groups might be attributed to temporary inhibitory effect of anaesthestic drug on renal blood flow and consequent decrease in the glomerular filtration rate, resulting rise in its level. It may also be due to increased levels of anti-diuretic hormones (Rabinowitz, 1969 and Church *et al*., 1994) [13, 2]. Similar findings have reported by Saini *et al*. (2017) [14] in dogs following administration of dexmedetomidine and thiopentone sodium anaesthesia.

Table 11: Showing effect of various anaesthetic protocol on serum urea nitrogen (mg/dL) in different groups at various time intervals. (Mean ± SE)

Parameter	Groups (n=6)	Post -Anaesthesia (Min.)				
		0	30	60	120	6hr
Serum Urea Nitrogen (mg/dl)	A	20.72±0.50^{Aa}	20.89±0.17^{Aa}	21.03±0.33^{Aa}	20.85±0.33^{Aa}	20.70±0.67^{Aa}
	B	21.61±0.67^{Aa}	21.85±0.67^{Aab}	22.28±0.33^{Aab}	22.32±0.33^{Aa}	21.60±0.33^{Aa}
	C	21.03±0.83^{Aa}	21.35±0.02^{Aa}	21.47±0.32^{Aab}	21.28±0.83^{Aa}	20.91±0.21^{Aa}

ABC-Values bearing different superscript vary significantly (P<0.05) between groups
abc- Values bearing different superscript vary significantly (P<0.05) within groups

(d) Serum Creatinine

In group BT, a non-significant increase in serum creatinine values was observed up to 120 min. from 1.07±0.33 to 1.18±0.67 mg/dL after administration of butorphanol-thiopentone sodium anaesthesia. Later on, the values returned to normalcy between 5- 6 hrs. In group DT, a non-significant increase in serum creatinine was recorded up to 120 min. interval after administration of dexmedetomidine-thiopentone sodium anaesthesia from 0.98±0.38 to 1.20±0.50 mg/dL. Later on, the values returned to near preadministration level by 6 hrs. In group AT, a non-significant increase from 1.10±0.63 to 1.28±0.23 mg/dL up to 120 min was reported after administration of acepromazine-thiopentone sodium anaesthesia (Table 12). Later on, the values returned to normalcy between 6 hrs. The transient increase in the level of creatinine might be attributed to the temporary inhibition effect of anaesthetic drugs 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 in dogs (Church *et al*., 1994) [2]. In the present study, the animals of Group DT and AT showed marginal increase in serum creatinine values upto 120 minutes interval of the study observation and then gradually approached the base line value by 6 hours. Plasma creatinine level is greatly dependent on the rate of urinary flow, urine formation and elimination. Any type of the renal insufficiencies results in elevation of creatinine level of blood. Similar observations were reported by Jadon *et al.* (1995) and Saini *et al*. (2017) [14] in dogs following administration of dexmedetomidine and thiopentone sodium anaesthesia.

Table 12: Showing effect of various anaesthetic protocol on serum creatinine (mg/dL) in different groups at various time intervals. (Mean ± SE)

Parameter	Groups (n=6)	Post -Anaesthesia (Min.)				
		0	30	60	120	6hr
Serum Creatinine (mg/dl)	A	1.07±0.33^{Aa}	1.11.±0.26^{Aa}	1.15±0.53^{Aa}	1.18±0.67^{Aa}	1.09±0.35^{Aa}
	B	0.98±0.38^{Aa}	1.06±0.67^{Aa}	1.13±0.13^{Aab}	1.20±0.50^{Aa}	1.00±0.37^{Aa}
	C	1.10±0.63^{Aa}	1.17±0.83^{Aa}	1.22±0.43^{Aa}	1.28±0.23^{Aa}	1.12±0.17^{Aa}

ABC-Values bearing different superscript vary significantly (P<0.05) between groups
abc- Values bearing different superscript vary significantly (P<0.05) within groups

(e) Aspartate amino transferase (AST)

There was a non-significant increase in AST values from 29.07±0.27 to 29.98±0.19 IU/L up to 120 minutes interval in Group DT animals which are anaesthetized with dexmedetomidine and thiopentone sodium anasesthesia. On the other hand, the increase in AST persisted up to 60 minutes from 30.07±0.17 to 32.16±0.45 IU/L and 32.12±0.19 to 32.93±0.34 IU/L in animals Group BT and Group AT (Table 13). The serum ALT showed a non-significant increase after anaesthesia in all the groups of animals. AST is a liver specific enzyme in canines and any damage or pathology involving the hepatic parenchyma allows the leakage of large amount of enzyme in the blood circulation. A marginal higher increase in the level of AST was seen with dexmedetomidine + thiopentone sodium (Group DT) and acepromazine + thiopentone sodium (Group AT) animals after anaesthesia as compared to butorphanol + thiopentone sodium (Group BT) animals respectively. The non-significant changes in the level of AST observed in this study indicate the minimum deleterious effect of the anaesthetic agents used in this study on liver. Similar findings have also been observed following anaesthesia with thiopentone in dog (Kassem *et al*., 2019 and Saini *et al*., 2019) [8, 15]. The values of AST did not show any significant changes within the group and between the groups.

Table 13: Showing effect of various anaesthetic protocol on AST (IU/L) in different groups at various time intervals. (Mean ± SE)

Parameter	Groups (n=6)	Post-Anaesthesia (Min.)				
		0	30	60	120	6hr
AST(IU/L)	A	30.07±0.17^{Aa}	31.12±0.42^{Aa}	30.16±0.45^{Aa}	29.32±0.17^{Aa}	30.08±0.58^{Aa}
	B	29.07±0.27^{Aa}	30.70±0.17^{Aa}	31.89±0.21^{Aa}	29.98±0.19^{Aa}	29.08±0.32^{Aa}
	C	32.12±0.19^{Aa}	33.57±0.32^{Aa}	33.93±0.34^{Aa}	32.42±0.17^{Ab}	32.09±0.50^{Aa}

ABC-Values bearing different superscript vary significantly (P<0.05) between groups
abc- Values bearing different superscript vary significantly (P<0.05) within groups

Alanine amino transferases (ALT)

There was a non-significant increase in total ALT values from 28.96±0.53 to 29.65±0.24 IU/L up to 120 minutes interval in the animals of Group DT which was anaesthetized with dexmedetomidine and thiopentone sodium. On the other hand, the increase in ALT value persisted up to 60 minutes in Group BT and AT from 29.99±0.83 to 30.64±0.72 IU/L and 29.64±0.67 to 29.99±0.15 IU/L which were administered with combination of butorphanol-thiopentone sodium and acepromazine-thiopentone sodium anaesthesia respectively (Table 14). When the liver damage occurs, then the membranes may become permeable or wall may rupture, thereby the enzymes diffuse into the blood stream and increased the level of alanine aminotransferase in the blood circulation (Koichev *et al*., 1988) [9]. Similarly, a non-significant increase in values of ALT has been reported in

dogs anaesthetized with dexmedetomidine and thiopentone sodium anesthesia (Saini *et al*., 2019) [15]. In the present study, the values of ALT did not revealed any significant changes within and between the groups.

Table 14: Showing effect of various anaesthetic protocol on ALT (IU/L) in different groups at various time intervals. (Mean ± SE).

Parameter	Groups (n=6)	Post -Anaesthesia (Min.)				
		0	30	60	120	6hr
ALT (IU/L)	A	29.99±0.83^{Aa}	30.28±0.23^{Aa}	30.64±0.72^{Aa}	30.31±0.53^{Aa}	29.92±0.43^{Aa}
	B	28.96±0.53^{Aa}	29.12±0.67^{Ba}	29.36±0.53^{Aa}	29.65±0.24^{Aa}	28.98±0.04^{Aa}
	C	29.64±0.67^{Aa}	29.85±0.33^{Aa}	29.99±0.15^{Aa}	29.68±0.61^{Aa}	29.60±0.38^{Aa}

ABC-Values bearing different superscript vary significantly (P<0.05) between groups
abc- Values bearing different superscript vary significantly (P<0.05) within groups

Conclusion

On the basis of above study, it was concluded that thiopentone sodium could be safely used for inducing general anaesthesia with butorphanol, dexmedetomidine and acepromazine in canines. However, the haemato-bichemical alterations observed during the study period were transient, well tolerated by the animals and soon returned to their pre administration level. These combinations of drugs did not produce any harmful effect on vital organs and the changes werew marginal which remained within physiological limits.

References

1 Bayan H, Sharma KK, Chakravarty P. Biochemical and haematological changes during propofol anaesthesia in canine. Indian J Vet. Surg. 2002;23(2):95-96.
2 Church DB, Nicholson AI, Illkiw 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.
3 Dollery SC. Therapeutic Drugs. Churchill Livingstone, London; c1991, p.21.
4 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 alpha-2-receptors. J Neuroimmunol. 1995;57:27-34.
5 Fulsunge RK, Thorat MG, Chepte SD, Fani FA, Bhave NP, Vaidya SR. *et al.* Anaesthetic efficacy of thiopental: Propofol admixture and propofol as total intravenous anaesthesia in dog. The Pharma Innovation Journal. 2019;8(9):404-407.
6 Hall LW, Clarke KW, Trim CM. Veterinary Anesthesia, 10th edition. Saunders, Elsevier Limited; c2001.
7 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.
8 Kassem M, Nasr, M, Sadik K, Belal S. The effect of intravenous administration of propofol, thiopental, or propofol plus thiopental mixture in dogs undergoing experimentally liver insufficiency. Damanhour Journal of Veterinary Sciences. 2019;2(2):19-23.
9 Koichev K, Golemanov D, Houbenov H, Aminoko B. Experimental study on effect of 'domosedan' in sheep and cattle. J Assoc. Vet. Anaesth. 1988;15:114-126.
10 Lim JH, Jang KH, Jang IH. Comparative effect of propofol or propofol and ketamine for the induction of anaesthesia in dogs. Vet. Rec. 2000;146(20):571-574.
11 Miller RD. Anaesthetic pharmacologic, Intravenous Anesthetics. En: Miller's Anesthesia. 7th Ed. Churchill Livingstone Elsevier; c2009, p.26.
12 Pircio AW, Gylys JA, Cavanagh RL, Buyniski JP, Bierwagen ME. The pharmacology of butorphanol, a 3, 14-dihydroxymorphinan narcotic antagonist analgesic. Archives Internationales de Pharmacodynamie Therapie. 1976;220(2):231-257.
13 Rabinowitz L. Effects of reduced GFR on the fractional excretion of urea in dog. Proc. Soc. Exp. Biol. Med. 1969;132:27-29.
14 Saini R, Jadon NS, Kandpal M, Bodh D. Studies on the effects of thiopental sodium with and without dexmedetomidine in dogs. Indian Journal of Veterinary Surgery. 2017;38(1):44-46.
15 Saini R, Jadon NS, Kandpal M, Kumar A. Clinicophysiological and haematobiochemical effects of dexmedetomidine as preanesthetic in combination with thiopental sodium and ketamine in dogs. The Pharma Innovation Journal. 2019;8(7):12-17.
16 Shaaban MF, Kassem MM, Kammar MH, Korittum SA. Clinical evaluation of intravenous propofol alone or in combination with diazepam, ketamine HCl and thiopental sodium to induce general anaesthesia in dogs. Alexandria J Vet. Sci. 2018;57(1):106-114.
17 Skarda RT, Muir WW. Caudal analgesia induced by epidural or subarachnoid administration of detomedine hydrochloride solution in mares. Am. J Vet. Res. 1996;57(2):193-200.
18 Soliman MK, Amrousi SE, Khamis MY. The influence of tranquilizers and barbiturate anaesthesia on the blood picture and electrolytes of dogs. Vet. Rec. 1965;77:1256-1259.
19 Turi AK, Muir WW. Pain assessment and management. Small Animal Pediatrics; c2011, p. 220-232.
20 Wagner AE, Muir WW, Hinchcliff FW. Cardiovascular effect of xylazine and detomidine in horses. Am. J Vet. Res. 1991;52:651-657.