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Anaesthetic efficacy of thiopental: Propofol admixture and propofol as total intravenous anaesthesia in dog

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Abstract
The present study was commenced to evaluate the anaesthetic efficacy of Propofol in comparison with Thiopental-Propofol 1:1 V/V admixture in 12 clinical canine patients presented for various surgical interventions. Irrespective of age, sex, breed and surgical intervention these cases were divided in two groups (n=6). In group A admixture of Thiopental-Propofol 1:1 V/V was used @ 7mg/kg body weight and in group B Propofol was used @ 4 mg/kg body weight. To evaluate the anaesthetic efficacy Assessment of anaesthesia, Clinico-physiological parameters and Haemato-Biochemical parameters were studied. Quality of anaesthesia was comparatively better in group A. There was a better cardiopulmonary stability in group A throughout study period as compared to group B with a significantly lower rectal temperature in group A. In haematological studies Hb, PCV, TEC exhibited a decreasing trend with Neutrophilia and lymphopenia in both groups. Biochemical parameters such as AST, ALT, BUN and creatinine were increased in group A, but were within normal physiological range throughout the period of study in both the groups. Group B showed significantly increased level of Glucose. The admixture of thiopental sodium and propofol 1:1 V/V can be safely implemented as general anaesthesia for various surgical interventions in dogs.

Keywords: Thiopental, propofol, admixture, general anaesthesia, dog

Introduction
General anaesthesia is a reversible, controlled drug-induced intoxication of central nervous system accompanied by muscle relaxation, in which the patient neither perceives nor recalls noxious or painful stimuli. An ideal anaesthetic is one which produces sleep, amnesia, muscle relaxation and analgesia. However, all these effects cannot be produced by the single agent and therefore a combination of drugs is used which is known as the balanced anaesthesia (Thurmon and Short, 2007, Arunkumar *et al*, 2017) [1, 2]. Balanced anaesthesia is a technique in which several drugs are combined at reduced dosages to decrease adverse effects of each drug and used to limit cardiopulmonary depression (Toner, 2005, Maravi*et al*, 2017) [3, 4]. Nowadays a major emphasis has been laid to develop new and safe injectable anaesthesia techniques, especially the 'Total Intravenous Anaesthesia' (TIVA), for the veterinary subjects primarily because of the fact that veterinary institutions are located outside the major cities where the facilities for inhalant anaesthesia are lacking. A technique of general anaesthesia which uses a combination of agents given exclusively by the intravenous route without the use of inhalation agents is called Total intravenous anaesthesia (TIVA). TIVA could lead to a faster recovery of cerebral function, which may lead to better behaviour and advantages in postoperative management.
Thiopental–Propofol admixture comprises of 1:1 V/V Thiopental 2.5% and Propofol 1%, when used together as admixture shows hypnotic synergism in patients (Naguib and Sari-kouzel., 1991) [5]. The admixture of Thiopental and Propofol is compatible and stable at operating room temperature (21˚ C-23 ^{0}C) while having a bactericidal and inhibitory effect on the growth of micro-organism for upto 24 hours (Lazar *et al.*, 1998) [6].
The Thiopental-Propofol admixture produces similar changes in echocardiographic variables when compared to Propofol or Thiopentone alone. There are studies indicating that Thiopental can be used together with Propofol for anaesthetic induction in canines. This mixture presents advantages of stability at room temperature, reduced support of bacterial growth, and absence of effect upon recovery profile. The dose of Propofol is markedly reduced when used as admixture along with Thiopental leading to decreased toxicity of the drug.

Addition of Thiopental also provides better analgesia and muscle relaxation in the anaesthetic protocol than Propofol alone.

Methodology

The present study was conducted on 12 clinical cases of dogs. Irrespective of the surgical procedure these clinical cases were randomly divided into two equal groups comprising of six animals in each group.

Group A (N=6): Admixture of Inj. Thiopental 2.5% (@ 5 mg/kg body weight) + Inj. Propofol 1% (@ 2 mg/kg body weight) 1:1 V/V as TIVA.

Group B (N=6): Inj. Propofol (@ 4mg/kg body weight) as TIVA.

All the animals of both groups were sedated with Inj. Xylazine @ 2 mg/kg body weight and Inj. Meloxicam @ 0.5 mg/kg body weight, Inj. Chlorphenaramine maleate @ 0.5 mg/kg body weight, Inj. Amoxicillin+ cloxacillin @ 15 mg/kg body weight were given intra-muscularly as premedication.

During the research trials, varoius surgical procedures like Ovario-hysterectomy, Orchiectomy, Tumour resection, Limb amputation and Vaginal fold Hyperplasia in bitch were performed.

Anaesthetic assessment was carried out by recording Quality of Anaesthesia, Induction time, Extubation time and Recovery time. Clinical observations like respiratory rate, heart rate and rectal temperature were evaluated during the surgical procedure up to 75 min. Venous blood samples were taken to estimate changes in various haemato-biochemical parameters occurring during the study. All haemato-biochemical parameters were recorded before induction (0 min), intra-operatively, at recovery and at 8 hours from recovery in all cases.

The data collected during the present study was statistically analysed by using Two Way Factorial Experimental Design as per ICAR WASP 2.0 software.

Results and Discussion

Assessment of anaesthesia

Anaesthetic assessment was evaluated on the basis of quality of anaesthesia, induction time, time taken for recovery and extubation time. The mean time for induction was significantly higher in group A (31.50±0.50 sec) than group B (27.83±0.3 sec), but in group A dose of propofol for induction was reduced by 50 %. Shorter time for induction in group B can be attributed to rapid uptake of propofol in central nervous system and also its high lipid solubility which facilitates in quick blood-brain barrier equilibrium (Lumb and Jones., 2007) [7a]. Difference in extubation time of both the groups was non-significant with mean being (15.83±2.41 min) and (16.50±1.50 min) for group B and group A respectively. Whereas recovery time was significantly shorter in group B with mean time of (12.67±1.02 min) while mean of group A was (20.33±1.02 min). The prolonged recovery in group A could be due to Thiopental manifested cumulative effect on anaesthesia which resulted in prolonged recovery time after repeated dosing (Lumb and Jones, 2007) [7b]. Quality of anaesthesia in both the groups was satisfactory but there was presence of palpebral reflex, and jaw muscle tone in two animals from the group B, whereas in group A all the clinical signs were absent indicating superior quality of anaesthesia. Inferior quality of Propofol as sole anaesthetic agent for TIVA can be attributed to its poor analgesic property. Hence, it is necessary to incorporate propofol with an anaesthetic drug which has analgesic and muscle relaxant property (Jena *et al.*, 2014) [8].

Table 1: Mean ± SE of Induction Time (seconds), Extubation time (Minutes) and Recovery Time (Minutes)

Group	Induction Time (Seconds)	Extubation Time (Minutes)	Recovery Time (Minutes)
Group A	31.50 ± 0.50^{b}	16.50±1.50	20.33 ± 1.02^{b}
Group B	27.83 ± 0.31^{a}	15.83±2.41	12.67 ± 1.02^{a}

Means bearing superscript differ significantly at 1% level of significance ($P< 0.01$).

Clinico-physiological parameters

Significant variation in pooled mean of both the groups at different intervals was evident for rectal temperature which ranged from 101.65±0.42 to 100.46±0.59°F and respiration rate which ranged from 16.92±2.19 to 11.50±1.19 breath per minute. The mean rectal temperature for group B was (101.7±0.16 °F) which was significantly greater than the mean values of group A (100.2±19.10 °F), this could be a result of decrement in basal metabolic rate, peripheral vasodilation, abated muscle tone and depression of thermoregulatory mechanisms produced by general anaesthesia (Manat, 2001) [9]. Similarly mean heart rate in group B was 54.24±1.48 beats per minute which was significantly lower than the mean heart rate values of group A being 62.26±2.03 beats per minute, this can be attributed to decreased sympathetic tone and increased vasodilation following propofol administration which is accompanied by attenuation of arterial baroreflex which resulted in only negligible increase in heart rate, whereas arterial baroreflex is unaltered after thiopental administration in dogs resulting in increased heart rate from baseline values (Manat 2001) [9].

Table 2: Mean ± SE of rectal temperature (Degree fahrenheit)

Time Interval	Rectal Temperature		Overall pooled Mean
	Group A	Group B	
0	101.20±0.65	102.10±0.51	101.65 ± 0.42^{II}
15	100.82±0.56	102.45±0.53	101.63 ± 0.44^{II}
30	100.45±0.40	101.97±0.70	101.21 ± 0.45^{I}
45	100.32±0.41	101.68±0.66	101 ± 0.42^{I}
60	99.77±0.66	101.47±0.63	100.62 ± 0.50^{I}
75	99.68±0.68	101.37±0.45	100.53 ± 0.47^{I}
Recovery	99.60±1.06	101.32±0.30	100.46 ± 0.59^{I}
Pooled Mean	100.2 ± 19.10^{A}	101.7 ± 0.16^{B}	

Means bearing superscripts differ significantly 1% ($P< 0.01$) and 5% ($P< 0.05$) level of significance.

Table 3: Mean ± SE of Heart rate (Beats/ minutes) and Respiration rate (Breath/ minutes).

Time Interval	Heart rate		Overall pooled mean	Respiration rate		Overall pooled mean
	Group A	Group B		Group A	Group B	
0	53.67±4.86	47.83±2.50	50.75±2.75	12.67±0.84	21.17±12.50	16.92 ± 2.19^{II}
15	57±6.83	55.83±4.02	56.42±3.78	10.50±1.31	12.50±2.03	11.50 ± 1.19^{I}
30	60±9.19	50±2.11	55±4.74	12±1.26	13.50±0.81	12.75 ± 0.75^{I}

45	65.67±10.10	56.50±5.18	61.08±5.58	12.67±1.33	13.17±1.28	12.92±0.88^{I}
60	65.67±11.70	52.17±2.83	58.92±6.09	13.33±1.50	11.83±1.64	12.58±1.08^{I}
75	66.67±11.20	57.50±2.73	62.08±5.67	14.33±1.58	12.50±1.28	13.42±1.01^{I}
Recovery	67.17±10.57	59.83±2.17	63.50±5.26	13.67±1.31	16.17±2.90	14.92±1.56^{II}
POOLED MEAN	62.26±2.03^{B}	54.24±1.48^{A}		12.74±0.47	14.40±1.24	

Means bearing superscripts differ significantly 5% (P<0.05) level of significance.

Haematological studies

In haematological observations Hb, TEC and PCV decreased significantly between the groups but were within normal physiological limits throughout the period of study rendering them clinically insignificant. The decrease in the haemoglobin and PCV level could be attributed to splenic pooling of blood constituents, shifting of fluids from extra vascular compartment to intravascular compartment to maintain normal cardiac output (Maravi *et al*, 2017) [4]. In DLC the mean values of neutrophil count differed significantly between the pooled mean of intervals of both the groups and it ranged from 70.99±2.65% to 79.69±1.60%, neutrophil count also manifested significant difference between the means of both the groups with the values being 71.06±2.26% and 78.53±1.79% for group A and B respectively. Lymphocyte count showed corresponding decrease to neutrophil count while the variation between the groups being significant. Eosinophil, basophil and Monocyte showed statistically significant variation between groups and within interval but as the values were within normal physiological limits throughout the period of study the variation was rendered clinically insignificant.

Table 4: Mean ± SE of Hb (gm/dL), PCV (%), TEC (X10^6 cu/mm) and DLC (%) of both the groups.

		Before Induction	Intra-operatively	At Recovery	8 hrs from Recovery	Pooled Mean
Haemoglobin	A	12.23±0.57	11.42±0.46	10.50±0.35	11.80±0.48	11.49±0.37^{A}
	B	14.73±1.62	13.28±1.23	12.57±1.03	14.23±1.57	13.70±0.48^{B}
Overall Pooled Mean		13.48±0.90	12.35±0.69	11.53±0.61	13.02±0.86	
PCV	A	38.95±1.11	36.04±0.67	33.13±0.70	36.98±0.52	36.28±1.21^{A}
	B	44.31±3.69	41.84±3.28	38.57±2.71	43.41±3.34	42.03±1.26^{B}
Overall Pooled Mean		41.63±2.00^{II}	38.94±1.82^{I}	35.85±1.57^{I}	40.19±1.88^{II}	
TEC	A	5.77±0.13	5.53±0.13	5.30±0.13	5.65±0.12	5.56±0.10^{A}
	B	7.86±0.63	7.35±0.56	7±0.51	7.79±0.60	7.50±0.20^{B}
Overall Pooled Mean		6.81±0.44	6.44±0.39	6.15±0.36	6.72±0.43	
Neutrophil	A	67.22±4.16	70.22±4.26	77.58±1.72	69.23±4.88	71.06±2.26^{A}
	B	74.73±2.79	81.30±2.78	82.07±2.61	76.60±2.57	78.68±1.79^{B}
Overall Pooled Mean		70.98±2.64^{I}	75.76±2.94^{I}	79.82±1.63^{II}	72.92±2.85^{I}	
Lymphocyte	A	22.60±0.81	21.13±0.86	18.53±0.30	21.97±1.32	21.06±0.90^{B}
	B	15.35±2.02	12.23±2.09	11.37±1.92	13.07±2.30	13.00±0.43^{A}
Overall Pooled Mean		18.98± 1.51	16.68±1.72	14.95±1.42	17.52±1.84	
Monocyte	A	7.33±2.30	7.08±3.10	2.67±1.09	6.83±2.94	5.98±1.11
	B	6.75±1.07	4.28±1.18	4.37±0.61	6.67±0.94	5.52±0.69
Overall Pooled Mean		7.04±1.21	5.68±1.64	3.52±0.65	6.75±1.47	
Eosinophil	A	0.30±0.05	1.22±0.25	0.95±0.38	1.90±0.79	1.60±0.32^{A}
	B	2.87±0.46	1.85±0.40	1.95±0.42	3.30±0.41	2.49±0.35^{B}
Overall Pooled Mean		2.61±0.64	1.53±0.25	1.45±0.31	2.60±0.47	
Basophil	A	0.30±0.05	0.35±0.11	0.27±0.04	0.23±0.03	0.29±0.02
	B	0.30±0.06	0.37±0.06	0.25±0.09	0.25±0.06	0.29±0.03
Overall Pooled Mean		0.3±0.04	0.35±0.06	0.26±0.05	0.3±0.04	

Means bearing superscripts differ significantly 1% (*P*< 0.01) and 5% (*P*< 0.05) level of significance.

Biochemical studies

It was observed that values of AST, ALT, BUN and Creatinine were significantly greater in group A with mean being 40.37±1.14 IU/L, 41.58±1.71IU/L, 18.25±0.39 mg/dl and 1.33±0.07 mg/dl respectively than group B where the mean for AST, ALT, BUN and Creatinine were 20.92±3.38 IU/L, 12.77±0.91 IU/L, 12.08±0.67 mg/dl and 0.94±0.08 mg/dl respectively. As all these values were within normal range the variation was clinically insignificant. Due to anaesthesia and stress associated with surgery release of aldosterone, vasopressin, renin and catecholamines occurred (Lumb and Jones, 2007) [7c]. Renal blood flow, glomerular filtration rate and urine production are generally decreased with surgery in any patient. This led to decreased excretion of these metabolites and their increased level in blood (Dinesh *et al*, 2019) [10]. Whereas, the blood glucose level was non-significantly higher in group B (110.47±14.14) mg/dl than group A (98.82±9.55) mg/dl. There was significant variation within intervals of both the groups which ranged from 79.75±7.02 mg/dl to 120.18±13.21 mg/dl in group A and for group B it ranged from 79.50±0.84 mg/dl to 144.46±8.56 mg/dl. Pooled mean of intervals of both the groups also varied significantly and it ranged from 79.63±3.37 mg/dl to 120.48±9.49 mg/dl. The increase in blood glucose levels in both the groups could be attributed to the stress related with anaesthesia which stimulates the hypothalamus and pituitary to release ACTH, this ACTH acts on adrenal glands to produce glucocorticoids which lead to production of glucose from muscle and liver glycogen causing hyperglycemia (Manat2001, Gupta2005) [9, 11].

Table 5: Mean ± SE of ALT (IU/L), AST (IU/L), BUN (mg/dL), Creatinine (mg/dL) and Glucose (mg/dL).

		Before Induction	Intra-operatively	At Recovery	8 hrs from Recovery	Pooled Mean
ALT	A	38.05±8.32	41.40±6.96	46.22±8.77	40.64±8.26	$41.58±1.71^{B}$
	B	14.35±0.71	13.98±0.94	10.35±0.65	12.40±0.86	$12.77±0.91^{A}$
Overall Pooled Mean		26.20±5.35	27.69±5.32	28.28±6.84	26.52±5.81	
AST	A	37.67±9.46	42.98±9.63	39.53±9.02	41.28±9.62	$40.37±1.14^{B}$
	B	19.40±3.45	16.79±1.96	16.62±0.59	30.90±4.02	$20.92±3.38^{A}$
Overall Pooled Mean		28.54±5.54	29.88±6.13	28.07±5.52	36.09±5.21	
BUN	A	17.39±1.27	18.41±1.28	19.24±1.56	17.95±1.29	$18.25±0.39^{B}$
	B	12.39±2.12	12.72±1.59	10.11±1.50	13.11±1.92	$12.08±0.67^{A}$
Overall Pooled Mean		14.89±1.40	15.57±1.30	14.68±1.72	15.53±1.32	
Creatinine	A	1.12±0.18	1.42±0.27	1.45±0.10	1.33±0.10	$1.33±0.07^{B}$
	B	0.88±0.10	1.18±0.12	0.79±0.08	0.90±0.08	$0.94±0.08^{A}$
Overall Pooled Mean		1±0.10	1.30±0.15	1.12±0.12	1.12±0.09	
Glucose	A	$79.75±7.02^{a}$	$109.37±12.23^{b}$	$120.18±13.21^{b}$	$86±3.92^{a}$	98.82±9.55
	B	$79.50±0.84^{a}$	$97.13±13.04^{a}$	$120.78±14.89^{b}$	$144.46±8.56^{b}$	110.47±14.14
Overall Pooled Mean		$79.63±3.37^{I}$	$103.25±8.72^{II}$	$120.48±9.49^{II}$	$115.23±9.89^{II}$	

Means bearing superscripts differ significantly 1% (P<0.01) and 5% (P<0.05) level of significance.

Conclusions

From the present study it can be concluded that the ratio of thiopental sodium and propofol 1:1 V/V used for induction and maintenance of general anaesthesia could be safely implemented for various surgical interventions in dogs. The dose of Propofol is markedly reduced when used as admixture along with Thiopental leading to decreased toxicity of the drug. Admixture of Thiopental and Propofol imparts better analgesia, muscle relaxation, provides a synergistic effect, better cardiopulmonary stability and alleviation of pain on intravenous injection. It reduced chances of bradycardia and apnoea in canine patients. Use of Thiopental and Propofol admixture for anaesthesia in canine is more cost-effective affair than Propofol anaesthesia.

References

1. Thurmon JC, Short CE. History and Overview of Veterinary Anesthesia. In: Tranquilli, W. J., Thurmon, J. C., Grimm, K. A. (Editors). Lumb and Jones' Veterinary Anesthesia and Analgesia. 4th Edn. Blackwell Publishing Ltd, Oxford, 2007, 3-6.
2. Arunkumar S, Dilipkumar D and BV Shivaprakash. Clinical and physiological evaluation of dexmedetomidine, xylazine and triflupromazine as pre-anaesthetics with propofol-isoflurane anaesthesia forvarious surgeries in dogs. The Pharma Innovation Journal. 2017; 6(8):100-105.
3. Toner PH. 'Balanced anaesthesia today', Best Practice and Research: Clinical Anaesthesiology. 2005; 19:475-484.
4. Maravi MS, Dewangan R, Tiwari SK, Sharda R. Haemato-biochemical response to detomidine-propofol combination in atropinized goats. The Pharma Innovation Journal. 2017; 6(11):312-315.
5. Naguib M, Sari-kouzel A. Thiopentone-propofol hypnotic synergism in patients, British journal of anaesthesia. 1991; 67:4-6.
6. Lazar ER, Jolly DT, Tam YK, Hrazdil J, Tawfik SR, Clanachan AS. Propofol and thiopental in a 1: 1 volume mixture is chemically stable. Anesthesia& Analgesia. 1998; 86(2):422-426.
7. Lumb A, Jones. Injectable and alternative anaesthetic technique. In: veterinary Anaesthesia and Analgesia. (William J. Tranquill, John C. Thurmon and Kurt A. Grimm eds.) 4th eds. Black well Publishing, 2007a, 291
8. Lumb, Jones. Injectable and alternative anaesthetic technique. In: veterinary Anaesthesia and Analgesia. (William J. Tranquill, John C. Thurmon and Kurt A. Grimm eds.) 4th eds. Black well Publishing, 2007b, 284.
9. Lumb, Jones. Renal disease. In: veterinary Anaesthesia and Analgesia. (William J. Tranquill, John C. Thurmon and Kurt A. Grimm eds.) 4th eds. Black well Publishing, 2007c, 915-920.
10. Jena B, Das J, Nath I, Sardar KK, Sahoo A, Beura SS *et al*. Clinical evaluation of total intravenous anaesthesia using Xylazine or dexmedetomidine with propofol in surgical management of canine patients. Veterinary World. 2014; 7(9):671-680.
11. Manat D. Studies on anaesthetic evaluation of propofol-thiopentone sodium as an induction and maintenance agent in dogs (*Canis domestica*), MVSc thesis Anand agriculture university, Gujarat, 2001.
12. Dinesh, Bisla RS, Tayal R, Chaudhary RN, Kumar A. Comparative evaluation of efficacy and safety of two balanced anaesthetic protocols in female dogs undergoing mammary tumor resection. The Pharma Innovation Journal. 2018; 7(8):286-292.
13. Gupta BB. Studies on certain anaesthetic techniques in dogs with special reference to Propofol. Ph d thesis Himachal Pradesh Krishivishvavidyalaya palampur-176062, Himachal Pradesh, 2005, 110.