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Clinical and physiological evaluation of dexmedetomidine, xylazine and triflupromazine as pre-anaesthetics with propofol-isoflurane anaesthesia for various surgeries in dogs

Arunkumar S, Dilipkumar D and BV Shivaprakash

Abstract
The research was conducted in 18 clinical cases presented to TVCC, Bidar. Animals were randomly divided into three groups viz., Group-I, Group-II and Group-III consisting of six animals in each group. Animals of all the groups were atropinised (0.045mg/kg) intramuscularly. Dogs in Group-I received dexmedetomidine (10µg/kg) intravenously. In the Group-II, xylazine (1mg/kg) was administered intravenously. In the Group-III, triflupromazine (1mg/kg) was administered intravenously. After ten minutes anesthesia was induced by propofol (3mg/kg) intravenously to each animal of all the groups. Maintenance of anesthesia was done by isoflurane in three groups. Anaesthetic combinations were evaluated by clinical and physiological observations. The induction and recovery were smooth and uneventful in three groups. Onset of sedation and induction time were narrowly quicker in Group-I. Excellent muscle relaxation and good analgesia were observed in group-II dogs. Physiological parameters fluctuated within the normal limits. Three anesthetic protocols in the present study provided satisfactory surgical plane of anesthesia in dogs.

Keywords: anesthesia, dog, dexmedetomidine, xylazine, triflupromazine, propofol, isoflurane

Introduction
Many minor and major surgical procedures are routinely performed in small animal practice that require short term sedation, analgesia or anaesthesia. Reversible production of insensibility to pain is known as anaesthesia. In veterinary practice, anaesthesia has to satisfy two requirements, humane handling of animals and technical efficiency. Anaesthesia is a indispensible pre-requisite for many surgical interventions with maximum technical efficiency and accuracy, so that surgeon can perform surgeries at ease. 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) [31].

Xylazine was the first alpha-2-adrenoceptor agonist used by veterinarians. It has been used as a pre-anaesthetic sedative before administration of injectable and inhalant anaesthesia and also reduce amount of injectable and inhalant anaesthesia required to produce the general anaesthesia.

Dexmedetomidine is the dextro-isomer of medetomidine that posses the selective alpha-2-agonist action because of its pharmacological activity. Triflupromazine is a phenothiazine derivative drug which is used most commonly as a pre-anaesthetic in dogs. Propofol (2,6 di-is opropylphenol) is a non-barbiturate hypnotic ultra-short acting anaesthetic with minimal analgesic, having rapid onset, short duration, lack of excitatory and cumulative effect on repeated administration (Buffalari *et al*., 1996). Inhalant anaesthetics for maintenance of a anaesthesia is preferred because of better quality and control over anaesthetic depth and ability to accurately titrate the dose administered (Pottie *et al*., 2007) [27] as compared to intravenous anaesthesia or even total intravenous anaesthesia.

Materials and Methods
The study was carried out in 18 clinical cases presented to TVCC, Bidar. The study was conducted to evaluate anaesthetic combinations of dexmedetomidine-propofol-isoflurane, xylazine-propofol-isoflurane and triflupromazine-propofol-isoflurane with various surgical conditions in dogs.

All the animals were kept off feed for 12hrs and water was withheld for 6hours prior to the anaesthesia. Eighteen clinical cases were randomly divided into three groups *viz*., Group-I, Group-II and Group-III with 6 animals in each group. Animals of all groups were atropinised at the dose rate of 0.045mg/kg body weight. The animals in Group-I received dexmedetomidine at the dose rate of 10µg/kg body weight intravenously, after ten minutes of dexmedetomidine administration, the anaesthesia was induced by administering propofol, at the dose rate of 3mg/kg body weight intravenously. In the animals of Group-II, xylazine was administered at the dose rate of 1mg per kg body weight intravenously, anaesthesia was induced by administering propofol intravenously, at the dose rate of 3mg/kg body weight. In the animals of Group-III, triflupromazine was administered at the dose rate of 1mg per kg body weight intravenously, anaesthesia was induced by administering propofol intravenously, at the dose rate of 3mg/kg body weight. After induction, maintenance of anaesthesia was carried under is of lurane inhalant anaesthetic.

Clinical and physiological parameters *viz*., Onset of sedation (noted with the onset of symptoms such as ataxia, drooping of eyelids and sleepiness), induction time (time taken for induction of general anaesthesia after propofol administration), duration of anaesthesia (time between the abolition and reappearance of pedal reflex), recovery time (time taken for animal to stand voluntarily after the cessation of anaesthesia) analgesia (measured by pin pricks on body and vigorous squeezing and twisting or pinching of digit or pad), palpebral (blink in response to a light tap on the medial or lateral canthus of eye) and pedal reflex (flexion or withdrawal of the limb in response to vigorous squeezing and twisting or pinching of digit or pad), muscle relaxation (relaxation of abdominal muscles and reduced resistance to passive flexion of the limb), heart rate, rectal temperature and respiratory rate were recorded before pre-anaesthetic administration (before) and 10 minutes after pre-anaesthetic administration and at 5, 15, 30, 60 minutes and 120 minutes interval after induction of anaesthesia.

The mean and standard error of all parameters were computed as per Snedecor and Cochran (1994) [30]. The variations in clinical and physiological parameters were recorded at different time intervals within the group and between the groups and were analyzed using student "t" test as described by Snedecor and Cochran (1994) [30].

Results and Discussion

When dexmedetomidine was used as a pre-anaesthetic for propofol-is of lurane anaesthesia, time for onset of sedation, induction time, duration of anaesthesia and recovery time were 2.05±0.19 minutes, 57.33±0.99 seconds, 94.17±11.50 minutes and 22.33±3.12 minutes respectively. Ahmad *et al*. (2012) [2] reported onset of sedation was 4.50±0.96 minutes after intramuscular injection of the dexmedetomidine. Alvaides *et al*. (2008) [3] reported level of sedation was increased within 2 to 5 minutes of dexmedetomidine administration. Clarke *et al*. (2014) stated onset of action of propofol was about 15 seconds and reached peak effect at 90 seconds after intravenous administration. Jena *et al*. (2014) [17] reported duration of anaesthesia and recovey period was 54.33±2.99 and 13.67±1.02 minutes respectively after administration of dexmedetomidine-propofol anaesthesia. Duration of anaesthesia was dependent on the length and need of the surgery.

When xylazine was used as a pre-anaesthetic for propofol-is of lurane anaesthesia, time for onset of sedation, induction time, duration of anaesthesia and recovery time were 3.33±0.48 minutes, 58.50±1.54 seconds, 67.17±12.50 minutes and 18.17±1.83 minutes respectively. Dewangan *et al.* (2010) [9] observed that administration of xylazine-propofol caused onset of sedation in 5.50±0.22 minutes. Jena *et al*. (2014) [17] reported duration of anaesthesia and recovery time 72.50±3.35 and 11.17±1.14 minutes respectively under xylazine-propofol anaesthesia in dogs.

When triflupromazine was used as a pre-anaesthetic for propofol-isoflurane anaesthesia, time for onset of sedation, induction time, duration of anaesthesia and recovery time were 7.08±0.64 minutes, 60.50±1.09 seconds, 73.67±14.36 minutes and 18.00±2.07 minutes respectively. Sharma and Bhargava (2007) [28] reported that onset of anaesthesia was 60.83±6.88 seconds after the administration of triflupromazine-propofol in dog. Adetunji *et al.* (2002) reported recovery time was 18.60 ± 2.30 minutes after the administration of propofol as repeat bolus in dogs. Hikasa *et al.* (2000) [13] reported that duration (Mean±S.D.) of anesthesia with isoflurane was 69.00±7.00 minutes. Mean end-tidal concentrations of isoflurane during maintenance anesthesia was 0.80±1.00 per cent in sheep.

Group I had quicker onset of sedation and narrowly quicker induction time when compared to the group II and group III. Dexmedetomidine had rapid onset of action owing to its lipophilic properties (Amarpal *et al*., 1996) [4]. The fast onset of sedation recorded in the present study confirmed to the observations made in earlier studies following the administration of medetomidine /dexmedetomidine (Amarpal *et al*., 1996 and Ahmad *et al*., 2011) [4, 2]. Standing recovery time was longer in group I dogs as compared to group II dogs, this might be due to rapid biotransformation of xylazine with elimination half-life of 30.1 minutes as compared with dexmedetomidine which is having elimination half-life of 47 minutes (Kuusela *et al*., 2000) [23].

Analgesia was good, with complete loss of pedal reflex, in three groups. However, analgesia was better in group II dogs than in group I and group III dogs. Complete loss of pedal reflex could be probably attributed to the action of propofol-isoflurane in three groups. Hunter *et al.* (1997) [16] stated alpha-2A-receptor, the predominant subtype in CNS, was responsible for the sedative, analgesic and sympatholytic effect. Lemke (2004) [24] opined that analgesic effects of alpha-2-agonists mediated by activation of heteroceptor (alpha-2- receptor located on noradrenergic neuron) located in the dorsal horn of the spinal cord. Locus ceruleus is the site of origin for the descending medullospinal noradrenergic pathway, known to be an modulator of nociceptive neurotransmission, stimulation of the alpha-2- adrenoceptors in this area terminates the propagation of pain signals leading to analgesia (Vanda and Marie, 2006) [32]. Analgesic action of dexmedetomidine is mainly through spinally at the spinal cord, stimulation of the alpha-2-receptors at the substansia gelatinosa of the dorsal horn leads to inhibition of the firing of nociceptive neurons (Kuraishi *et al*., 1985) [22]. In group III dogs analgesic effects could be probably attributed to the propofol and isoflurane.

Palpebral reflex was completely abolished during surgical plane of anaesthesia in three groups. Similar findings observed by Kandpal *et al.* (2005) [18] and Dewangan *et al.* (2010) [9] under xylazine-propofol anaesthesia in dogs. Pedal reflex was completely abolished during surgical plane of

anaesthesia in the dogs of Group I, II and III which is in agreement with Kulkarni *et al*. (2006) [21] under propofol anaesthesia, Dewangan *et al.* (2010) [9] under xylazine-propofol anaesthesia and Gupta (2010) [12] under dexmedetomdine-butorphanol-propofol anaesthesia in dogs.

Muscle relaxation was good in all three groups of dogs during the study period. Greater muscle relaxation was observed in group II dogs than group I and group III dogs. The results of present study concurred with the observations of earlier researcher, who reported greater muscle relaxation and agreement with Mane *et al*. (2014) [25] under xylazine-ketamine-isoflurane in horse. Xylazine produces muscle relaxation mainly by inhibition of intraneural transmission within the central nervous system (Brikas *et al*., 1987) [6].

The rectal temperature decreased non-significantly in group I dogs, except at 10min where non-significant increase in rectal temperature observed. The rectal temperature decreased non-significantly in group II and group III dogs. Similar findings were observed by Sharma and Bhargava (2007) [28] in dogs under triflupromazine-propofol anaesthesia. Significant decrease in rectal temperature recorded by Kandpal *et al.* (2005) [18] in dogs after xylazine administration and it might be attributed due to decreased metabolic rate, muscle relaxation and direct depressant action on central nervous system.

Respiratory rate decreased significantly (P≤0.01) throughout the study period in three groups, except at 120 minutes, 10 minutes and 60 minutes interval, where the decrease was non-significant (P≥0.05) in group I, II and III respectively. Similar findings observed by Kandpal *et al.* (2005) [18], it might be attributed due to the direct depressant action on central nervous system. Kulkarni *et al.* (2006) [21] also reported that respiratory rate, significantly decreased under propofol anaesthesia in dogs. Similar findings were observed by Hikasa *et al.* (2000) [13] and Genccelep *et al*. (2004) [10] during isoflurane anaesthesia in sheep.

Heart rate decreased non-significantly throughout the study period in group I, except at 10 minutes interval, where it was increased significantly and at 5 minutes interval after propofol induction, the increase was non-significant. Similar findings were observed by Bloor *et al.* (1992) [5] and Pagel *et al*. (1998) [26] after dexmedetomidine administration. However, bradycardia induced by dexmedetomidine was modurated by atropine which was stated by Hogue *et al*. (2002) [14]. In group II and III non-significant increase in heart rate observed throughout the study period.

However, bradycardia induced by xylazine was prevented by prior administration of atropine sulphate opined by Klide *et al*. (1975) [20] and Hsu *et al*. (1985) [15]. Atropine increases heart rate by an early central stimulation of the vagal centre followed by a peripheral blocking action opined by Shutt and Bowes (1979) [29]. Similar findings observed by Sharma and Bhargava (2007) [28] under triflupromazine-propofol anaesthesia. Heart rate increased was observed by Keegan and Greene (1993) [19] under isoflurane anaesthesia in dogs.

Conclusion

Onset of sedation and induction were narrowly quicker and recovery was slow in dexmedetomidine-propofol-isoflurane (group I) anaesthesia than xylazine-propofol-isoflurane (group II) and triflupromazine-propofol-isoflurane anaesthesia (group III) in dogs. Physiological parameters like rectal temperature and heart rate showed no significant variation in three groups. Respiratory rate decreased significantly in three groups which was transitory in nature hence three combinations were well tolerated by the dogs.

Table I: Mean ± SE of clinical parameters at different intervals in dogs of group I, II and III

Parameter	Group	Mean±SE
Onset of Sedation (minutes)	Group I	2.05±0.19[a]
	Group II	3.33±0.48[b]
	Group III	7.08±0.64[c]
Induction Time (seconds)	Group I	57.33±0.99
	Group II	58.50±1.54
	Group III	60.50±1.09
Duration of Anaesthesia (minutes)	Group I	94.17±11.50
	Group II	67.17±12.50
	Group III	73.67±14.36
Recovery Time (minutes)	Group I	22.33±3.12
	Group II	18.17±1.83
	Group III	18.00±2.07

Values bearing superscript [a, b, c] differ significantly from each other at P≤0.05 level

Table II: Mean ± SE of physiological parameters at different intervals in dogs of group I, II and III

SL. No	Parameter	Time	Group I	Group II	Group III
1	Rectal Temperature (^{0}F)	0min	101.87±0.12	101.97±0.37	101.98±0.31
		10min	102.18±0.46	101.62±0.30	101.87±0.41
		5min	101.98±0.52	101.65±0.45	101.08±0.38
		15min	101.50±0.69	101.83±0.44	100.80±0.51
		30min	101.05±0.75	101.58±0.55	100.80±0.54
		60min	100.22±0.92	101.82±0.54	100.77±0.49
		120min	100.52±0.75	101.15±0.61	101.35±0.06
2	Respiratory Rate (Breaths/min)	0min	49.00±9.23	55.67±10.39	64.67±11.28
		10min	15.83±1.05**[a]	21.17±3.39*	32.50±4.41*[c]
		5min	13.83±1.38**	15.50±2.94**	17.50±3.33**
		15min	12.17±1.97**	16.50±3.24**	18.17±2.79**
		30min	12.17±2.36**[a]	18.67±3.40**	20.50±2.09**[c]
		60min	15.00±1.71**[a]	29.83±4.01*[b]	29.83±5.68*[b]
		120min	28.00±5.42	41.00±6.98	43.83±4.92
3	Heart Rate (Beats/min)	0min	92.67±2.63	85.50±9.00	97.00±13.83
		10min	127.00±9.75**	106.50±15.04	134.00±23.25
		5min	98.83±3.42	110.50±14.50	132.17±19.48
		15min	88.83±7.57	115.33±13.57	122.33±19.09
		30min	81.83±4.42[a]	108.50±14.66	116.83±11.63[c]
		60min	87.17±3.29	92.83±15.04	110.50±11.22
		120min	91.00±3.89	106.00±12.21	109.17±11.70

Values bearing superscript*differ significantly (P≤0.05) from interval 'before' within the group.
Values bearing superscript**differ significantly (P≤0.01) from interval 'before' within the group.
Values bearing superscript [a,b,c] differ significantly (P≤0.05) level between groups at corresponding intervals

Table III: Muscle relaxation at different intervals in dogs of group I, II and III

Sl. No	Group	Case no	Interval						
			Dexmedetomidine		Propofol-Isoflurane				
			0min	10min	5min	15min	30min	60min	120min
1	I	1	0	1	2	3	3	2	0
		2	0	1	1	2	2	1	0
		3	0	1	1	2	2	1	0
		4	0	1	3	3	2	1	0
		5	0	2	2	2	3	1	0
		6	0	1	2	2	2	1	0
Mean±SE			0.00±0.00	1.17±0.17^{**a}	1.83±0.30^{**a}	2.33±0.21^{**a}	2.33±0.21^{**a}	1.17±0.17^{**a}	0.00±0.00
2	II		Xylazine		Propofol-Isoflurane				
		1	0	2	2	3	3	2	0
		2	0	2	3	3	2	2	0
		3	0	2	3	3	3	3	0
		4	0	3	3	3	3	2	0
		5	0	1	2	2	3	2	0
		6	0	2	3	3	3	1	0
Mean±SE			0.00±0.00	2.00±0.26^{**b}	2.67±0.21^{**b}	2.83±0.17^{**a}	2.83±0.17^{**a}	2.00±0.26^{**b}	0.00±0.00
3	III		Triflupromazine		Propofol-Isoflurane				
		1	0	0	1	1	2	1	0
		2	0	0	1	2	1	1	0
		3	0	0	1	1	2	1	0
		4	0	0	1	2	2	1	0
		5	0	0	1	2	2	1	0
		6	0	0	2	2	1	0	0
Mean±SE			0.00±0.00	0.00±0.00^{c}	1.17±0.17^{**a}	1.67±0.21^{**c}	1.67±0.21^{**c}	0.83±0.17^{**a}	0.00±0.00

0 - Absence of muscle relaxation **1** - Mild muscle relaxation
2 - Moderate muscle relaxation **3** - Excellent muscle relaxation
Values bearing superscript*differ significantly (P≤0.05) from interval 'before' within the group.
Values bearing superscript**differ significantly (P≤0.01) from interval 'before' within the group.
Values bearing superscript **a,b,c** differ significantly (P≤0.05) level between groups at corresponding intervals

Table IV: Analgesia score at different intervals in dogs of group I, II and III

Sl. No	Group	Case no	Interval						
			Dexmedetomidine		Propofol-Isoflurane				
			0min	10min	5min	15min	30min	60min	120min
1	I	1	0	2	3	3	3	2	0
		2	0	2	2	2	2	2	0
		3	0	1	2	2	2	2	0
		4	0	1	2	3	3	2	0
		5	0	2	2	2	3	2	0
		6	0	1	2	2	2	1	0
Mean±SE			0.00±0.00	1.50±0.22^{**a}	2.17±0.17**	2.33±0.21**	2.50±0.22**	1.83±0.17**	0.00±0.00
2	II		Xylazine		Propofol-Isoflurane				
		1	0	3	3	3	3	2	0
		2	0	2	3	3	3	3	0
		3	0	3	3	3	3	2	0
		4	0	2	2	2	3	3	0
		5	0	3	3	3	3	2	0
		6	0	3	2	3	2	2	0
Mean±SE			0.00±0.00	2.67±0.21^{**a}	2.67±0.21^{**a}	2.83±0.17^{**a}	2.83±0.17^{**a}	2.33±0.21^{**a}	0.00±0.00
3	III		Triflupromazine		Propofol-Isoflurane				
		1	0	1	2	2	2	2	0
		2	0	1	1	2	2	1	0
		3	0	1	2	2	2	2	0
		4	0	1	1	2	2	1	0
		5	0	0	2	2	3	1	0
		6	0	1	2	2	2	1	0
Mean±SE			0.00±0.00	0.83±0.17^{**c}	1.67±0.21^{**b}	2.00±0.00^{**b}	2.17±0.17^{**b}	1.33±0.21^{**b}	0.00±0.00

(0) No analgesia; (1) Mild analgesia; (2) Moderate analgesia; (3) Excellent analgesia.
Values bearing superscript*differ significantly (P≤0.05) from interval 'before' within the group.
Values bearing superscript**differ significantly (P≤0.01) from interval 'before' within the group.
Values bearing superscript **a,b,c** differ significantly (P≤0.05) level between groups at corresponding intervals

Table V: Palpebral reflex score at different intervals in dogs of group I, II and III

Sl. No	Group	Case no	Interval						
			Dexmedetomidine		Propofol-Isoflurane				
			0min	10min	5min	15min	30min	60min	120min
1	I	1	+++	+	-	-	-	++	+++
		2	+++	+	-	-	-	+	+++
		3	+++	+	-	-	-	++	+++
		4	+++	+	-	-	-	++	+++
		5	+++	+	-	-	-	+	+++
		6	+++	+	-	-	-	++	+++
2	II		Xylazine		Propofol-Isoflurane				
		1	+++	+	-	-	-	++	+++
		2	+++	+	-	-	-	++	+++
		3	+++	+	-	-	-	+	+++
		4	+++	+	-	-	-	++	+++
		5	+++	+	-	-	-	+	+++
		6	+++	+	-	-	-	++	+++
3	III		Triflupromazine		Propofol-Isoflurane				
		1	+++	+++	-	-	-	++	+++
		2	+++	+++	-	-	-	++	+++
		3	+++	+++	-	-	-	+	+++
		4	+++	+++	-	-	-	++	+++
		5	+++	+++	-	-	-	++	+++
		6	+++	+++	-	-	-	++	+++

(+++) - Complete presence of reflex **(++)** - Moderate presence of reflex
(+) - Mild presence of reflex **(-)** - Complete absence of reflex

Table VI: Pedal reflex at different intervals in dogs of group I, II and III

Sl. No	Group	Case no	Interval						
			Dexmedetomidine		Propofol-Isoflurane				
			0min	10min	5min	15min	30min	60min	120min
1	I	1	+++	++	-	-	-	++	+++
		2	+++	+	-	-	-	++	+++
		3	+++	++	-	-	-	++	+++
		4	+++	+	-	-	+	+++	+++
		5	+++	++	-	-	-	++	+++
		6	+++	++	-	-	-	++	+++
2	II		Xylazine		Propofol-Isoflurane				
		1	+++	++	-	-	-	++	+++
		2	+++	++	-	-	+	++	+++
		3	+++	++	+	-	-	++	+++
		4	+++	++	-	-	+	++	+++
		5	+++	+	-	-	-	++	+++
		6	+++	++	-	-	-	+++	+++
3	III		Triflupromazine		Propofol-Isoflurane				
		1	+++	++	-	-	-	++	+++
		2	+++	++	-	-	-	++	+++
		3	+++	++	+	-	-	++	+++
		4	+++	++	-	-	-	++	+++
		5	+++	++	-	-	-	++	+++
		6	+++	+++	-	-	-	+++	+++

(+++) - Complete presence of reflex **(++)** - Moderate presence of reflex
(+) - Mild presence of reflex **(-)** - Complete absence of reflex

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