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Evaluation of sedative effect of dexmedetomidine with atropine sulphate as preanaesthetic agents on thiopentone/propofol as induction and isoflurane as maintenance anaesthetic agents in dogs

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Abstract

The present clinical study was conducted to assess the sedative effect of dexmedetomidine with atropine sulphate as preanaesthetic agents on thiopentone sodium or propofol as induction and isoflurane as maintenance anaesthetic agents in dogs based on evaluation of anaesthetic, clinico-physiological and haemato-biochemical parameters. Twelve clinical cases of dogs presented for surgical interventions were randomly divided into two groups with the objective to develop a safe anaesthetic protocol. All dogs were premedicated with atropine sulphate @ 0.02 mg/kg intramuscularly and dexmedetomidine @ 5 µg/kg intravenously. Anaesthesia was induced by intravenous administration of 2.5% thiopentone sodium in group I and 1% propofol in group II till effect and maintained by isoflurane with 100% oxygen throughout the surgery. Dexmedetomidine showed potent dose sparing effects on induction dose of thiopentone sodium and propofol. Sedation quality was excellent with smooth induction and rapid recovery without any complication in both the groups. Both combinations produced adequate analgesia, muscle relaxation and sufficient anaesthetic depth to perform surgery. No significant difference was observed in the clinico-physiological and haemato-biochemical parameters in both the groups.

Keywords: Atropine, dexmedetomidine, dogs, isoflurane, propofol, thiopentone

Introduction

The use of anticholinergic and sedative agents prior to induction of anaesthesia enhances quality of induction and reduces the deleterious effects of specific anaesthetic agent (Lemke, 2007) [1]. Atropine sulphate and glycopyrrolate are commonly used anticholinergics in canine veterinary practice to prevent bradycardia, decrease airway and salivary secretions, dilate pupils, block vagally mediated reflexes and block the effects of parasympathomimetic drugs (Lerche, 2015) [2]. Atropine sulphate decreases bradycardia induced by dexmedetomidine (Hogue *et al.*, 2002) [3]. Alpha-2 agonist have a major role in reducing the dose of subsequent anaesthetic agents. Dexmedetomidine is a highly selective and potent Alpha-2 adrenoceptor agonist (Kuusela *et al.*, 2000) [4]. It is twice potent to medetomidine and 40 times more potent than xylazine (Alvaides *et al.*, 2008) [5]. When used as preanaesthetic prior to general anaesthesia, it reduces induction doses of propofol and thiopentone sodium in canines (Villamandos *et al.*, 2006) [6] and (Saini *et al.*, 2017) [7]. Thiopentone sodium is an ultra-short acting barbiturate used with various preanaesthetic combinations for induction of anaesthesia in canines (Hall *et al.*, 2001) [8]. Propofol is a shorting acting intravenous induction as well maintenance anaesthetic agent in dogs. It has poor analgesic property hence it must be supplemented with an analgesic agent such as opioids or Alpha-2 agonist (Kilic, 2004) [9]. Isoflurane is commonly used inhalant anaesthetic having short induction and recovery time with less myocardial depressant properties (Steffey and Mama, 2007) [10]. The present study was undertaken to evaluate the sedative effect of dexmedetomidine with atropine sulphate as premedication on thiopentone sodium or propofol as induction and isoflurane as maintenance anaesthetic agents based on assessment of anaesthetic, clinico-physiological and haemato-biochemical parameters in dogs at different time interval.

Materials and Methods

The anaesthetic study was conducted in 12 clinical cases of dogs undergoing various surgical procedures irrespective of age, breed, sex and body weight. All the dogs were randomly divided into two groups consisting of six animals in each group.

The animals were kept off feed for 12 hours and water was withheld for 6 hours prior to surgical intervention. All the animals were premedicated with atropine sulphate @ 0.02 mg/kg body weight intramuscularly followed by dexmedetomidine @ 5 µg/kg body weight intravenously with 10 minutes interval between them. After five minutes of dexmedetomidine administration, anaesthesia was induced by intravenous administration of 2.5% thiopentone sodium in group I and 1% propofol in group II till effect. After achieving desire depth of induction, endotracheal intubation was performed in all animals of both the groups and anaesthesia was maintained by using 1.5% isoflurane along with 100% oxygen.

Both the anaesthetic protocols were evaluated on basis of dose sparing effect of dexmedetomidine on induction anaesthetics (Thiopentone/Propofol), recovery period, quality of sedation, induction, maintenance anaesthesia (jaw tone, pedal reflex, palpebral reflex and eyeball position) and quality of recovery (Singh *et al.*, 2012) [11]. The clinico-physiological parameters *viz.*, rectal temperature (°F), respiration rate (breaths/min), pulse rate (beats/min), systolic, diastolic and mean arterial blood pressure (mm Hg) and saturation of

peripheral oxygen (%) were recorded prior to administration of any preanaesthetic agent, after induction of anaesthesia and thereafter at every 15 minutes intervals up to 60 minutes using vital signs monitor. Blood samples were collected prior to administration of any preanaesthetic agent, after induction of anaesthesia and thereafter at every 15 minutes intervals up to 60 minutes for haemato-biochemical studies. Haematological parameters *viz.*, haemoglobin (g%), packed cell volume (%), total erythrocyte count (million/cu.mm), total leucocyte count (thousand/cu.mm) and differential leucocyte count (%) were estimated using automatic haemato-analyzer within 90 minutes of blood collection. Blood glucose (mg/dl) was measured by glucometer immediately after blood collection. Biochemical parameters *viz.*, total protein (g/dl), alanine amino transferase (IU/L), blood urea nitrogen (mg/dl) and creatinine (mg/dl) were analyzed using semi-automatic biochemical analyzer and standard kits.

Obtained statistical data were analyzed using R software version 4.0.3 to estimate the means and standard errors. Means were compared using analysis of variance (ANOVA) and Duncan's New Multiple Range Test (DNMRT).

Table 1: Mean ± values of various clinico-physiological parameters in both groups at different time intervals.

Parameters	Group	Before Preanaesthetics	After Induction	15 min. after induction	30 min. after induction	45 min. after induction	60 min. after induction	P value
Rectal Temperature (°F)	I	100.77±0.2 ^a	99.62±0.47 ^{ab}	98.35±0.55 ^{bc}	97.13±0.59 ^{cd}	96.15±0.67 ^{de}	94.93±0.84 ^e	5.04x10 ^{-7**}
	II	100.57±0.3 ^a	99.53±0.44 ^{ab}	98.35±0.43 ^{bc}	97.58±0.41 ^{cd}	96.97±0.47 ^{de}	96.23±0.48 ^e	3.15x10 ^{-7**}
Respiration rate (breaths/minute)	I	26.67±2.42 ^a	10.33±0.99 ^b	10.50±1.12 ^b	10.50±1.67 ^b	9.33±1.31 ^b	10.00±1.32 ^b	1.5x10 ^{-8**}
	II	27.83±2.59 ^a	10.17±1.3 ^b	9.50±0.67 ^b	9.00±0.58 ^b	9.33±0.49 ^b	8.67±1.15 ^b	3.6x10 ^{-11**}
Pulse Rate (beats/minute)	I	98.33±1.65 ^a	82.33±4.77 ^b	95.33±4.05 ^a	96.83±4.45 ^a	94.50±2.62 ^a	93.50±1.91 ^a	0.04 [*]
	II	99.50±2.39 ^a	89.83±1.62 ^c	97.17±2.06 ^{ab}	96.50±2.47 ^{ab}	94.83±1.3 ^{abc}	92.33±2.14 ^{bc}	0.03 [*]
Systolic Blood Pressure (mm Hg)	I	138.67±6.44 ^a	146.17±7.07 ^a	138.50±9.81 ^a	126.17±10.43 ^a	135.67±6.62 ^a	137.17±8.26 ^a	0.69
	II	133.00±6.61 ^a	140.67±5.53 ^a	136.50±5.66 ^a	124.17±7.67 ^a	128.17±8.53 ^a	135.67±8.38 ^a	0.63
Diastolic Blood Pressure (mm Hg)	I	84.00±6.07 ^a	102.83±6.52 ^a	88.33±9.47 ^a	82.33±10.2 ^a	91.17±9.5 ^a	93.83±9.28 ^a	0.6
	II	82.17±7.01 ^a	95.50±7.63 ^a	88.00±5.32 ^a	86.33±7.78 ^a	88.83±10.27 ^a	92.83±11.29 ^a	0.9
Mean Arterial Pressure (mm Hg)	I	100.83±5.95 ^a	116.17±6.27 ^a	104.17±9.38 ^a	97.33±10.01 ^a	104.00±7.32 ^a	107.00±8.93 ^a	0.68
	II	95.67±7.76 ^a	112.83±7.45 ^a	101.33±4.49 ^a	96.50±7.53 ^a	101.83±9.24 ^a	108.17±9.13 ^a	0.6
SPO ₂ (%)	I	96.17±0.75 ^a	98.17±0.48 ^a	95.00±1.06 ^a	96.00±1.29 ^a	95.83±1.42 ^a	95.50±0.89 ^a	0.38
	II	97.00±0.73 ^a	97.50±0.62 ^a	96.33±0.71 ^a	96.33±1.2 ^a	96.33±1.58 ^a	95.83±1.17 ^a	0.9
Capillary Refill Time (Seconds)	I	2.00±0 ^a	2.00±0 ^a	1.83±0.3 ^a	2.17±0.17 ^a	2.17±0.17 ^{aA}	2.00±0.26 ^a	0.82
	II	2.00±0 ^a	2.00±0 ^a	2.00±0.26 ^a	2.00±0 ^a	1.83±0.17 ^{aA}	2.00±0.00 ^a	0.91

Means bearing different superscripts differ significantly within the group (*p* < 0.05)

* *p* < 0.05; ***p* < 0.01

Table 2: Mean ± values of various haematological parameters in both groups at different time intervals.

Parameters	Group	Before Preanaesthetics	After Induction	15 min. after induction	30 min. after induction	45 min. after induction	60 min. after induction	P value
Haemoglobin (g %)	I	12.97±0.51 ^a	11.65±0.49 ^{ab}	10.97±0.47 ^b	10.32±0.49 ^b	10.12±0.62 ^b	10.02±0.88 ^b	0.01 [*]
	II	13.10±0.81 ^a	11.92±0.7 ^{ab}	10.65±0.71 ^b	10.75±0.81 ^b	9.98±0.59 ^b	10.37±0.84 ^b	0.04 [*]
Packed Cell Volume (%)	I	38.77±1.52 ^a	35.07±1.44 ^{ab}	33.03±1.35 ^b	31.37±1.56 ^b	30.57±1.87 ^b	30.25±2.75 ^b	0.01 [*]
	II	39.05±2.46 ^a	35.63±2.12 ^{ab}	31.92±2.13 ^b	32.05±2.39 ^b	29.85±1.82 ^b	30.90±2.61 ^b	0.03 [*]
Total Erythrocyte Count (million/cu.mm)	I	6.67±0.25 ^a	6.10±0.28 ^{ab}	5.67±0.22 ^{bc}	5.37±0.25 ^{bc}	5.09±0.32 ^c	5.01±0.35 ^c	0.001 ^{**}
	II	6.73±0.6 ^a	6.38±0.3 ^a	5.52±0.28 ^{ab}	5.16±0.39 ^b	5.07±0.35 ^b	4.97±0.4 ^b	0.01 [*]
Total Leukocyte Count (thousand/cu.mm)	I	14.73±0.81 ^a	13.43±1.1 ^{ab}	11.48±0.82 ^{bc}	10.07±0.55 ^{cd}	8.53±0.27 ^d	8.27±0.85 ^d	3.23 x 0 ^{-6**}
	II	14.80±2.13 ^a	13.18±2.67 ^a	11.60±2.7 ^a	10.35±2.81 ^a	9.63±2.46 ^a	8.62±2.04 ^a	0.51
Neutrophils (%)	I	88.17±2.32 ^a	86.00±1.84 ^{ab}	84.0±1.67 ^{abc}	79.50±1.2 ^c	78.17±2.21 ^c	82±1.88 ^{bc}	0.005 ^{**}
	II	85.00±3.03 ^a	84.17±3.12 ^a	83.33±2.87 ^a	81.83±2.57 ^a	81.17±2.7 ^a	82.33±1.8 ^a	0.92
Lymphocytes (%)	I	9.50±2.35 ^b	11.33±1.91 ^{ab}	12.33±1.15 ^{ab}	15.50±1.02 ^a	16.67±1.76 ^a	14.33±1.63 ^{ab}	0.04 [*]
	II	11.50±2.43 ^a	12.00±2.49 ^a	13.00±2.72 ^a	14.33±2.44 ^a	15.33±2.19 ^a	13.67±1.45 ^a	0.86
Monocytes (%)	I	1.67±0.21 ^b	2.00±0.26 ^b	2.67±0.49 ^{ab}	4.17±0.54 ^a	4.33±0.84 ^a	3.17±0.6 ^{ab}	0.005 ^{**}
	II	2.00±0.45 ^a	2.50±0.72 ^a	2.67±0.33 ^a	3.00±0.37 ^a	2.50±0.56 ^a	3.33±0.33 ^a	0.49
Eosinophils (%)	I	0.67±0.21 ^a	0.67±0.21 ^a	1.00±0.26 ^a	0.83±0.4 ^a	0.83±0.17 ^a	0.50±0.22 ^a	0.8
	II	1.50±0.43 ^a	1.33±0.21 ^a	1.5±0.34 ^a	0.83±0.4 ^a	1.00±0.26 ^a	0.67±0.21 ^a	0.32
Blood Glucose (mg/dl)	I	83.50±7.83 ^{ab}	74.00±5.89 ^b	76.00±2.74 ^b	78.83±6.31 ^b	82.83±3.63 ^{ab}	98.17±6.82 ^a	0.08
	II	86.17±2.65 ^{ab}	70.50±4.6 ^b	76.17±4.32 ^b	83.33±5.63 ^{ab}	85.83±8.29 ^{ab}	97.67±7.13 ^a	0.05

Means bearing different superscripts differ significantly within the group (*p* < 0.05)

* *p* < 0.05; ***p* < 0.01

Table 3: Mean \pm values of various biochemical parameters in both groups at different time intervals.

Parameters	Group	Before Preanaesthetics	After Induction	15 min. after induction	30 min. after induction	45 min. after induction	60 min. after induction	P value
Total Protein (g/dl)	I	8.25 \pm 0.25 ^a	7.92 \pm 0.23 ^a	7.41 \pm 0.37 ^{ab}	6.83 \pm 0.46 ^{bc}	6.45 \pm 0.33 ^{bc}	6.26 \pm 0.19 ^c	3.5 x 10 ^{-4**}
	II	7.92 \pm 0.35 ^a	7.54 \pm 0.27 ^a	6.93 \pm 0.27 ^{ab}	6.56 \pm 0.6 ^{ab}	6.08 \pm 0.57 ^b	6.02 \pm 0.47 ^b	0.02*
Alanine Amino Transferase (IU/L)	I	31.49 \pm 3.33 ^a	31.41 \pm 3.39 ^a	27.83 \pm 2.3 ^a	27.02 \pm 2.19 ^a	27.01 \pm 2.61 ^a	27.11 \pm 1.95 ^a	0.66
	II	29.21 \pm 3.38 ^a	27.27 \pm 3.23 ^a	21.86 \pm 3.71 ^a	23.38 \pm 2.01 ^a	23.62 \pm 1.03 ^a	22.33 \pm 1.5 ^a	0.33
Blood Urea Nitrogen (mg/dl)	I	15.25 \pm 1.71 ^a	16.36 \pm 2.1 ^a	14.73 \pm 1.66 ^a	14.98 \pm 2.0 ^a	14.42 \pm 1.62 ^a	14.34 \pm 1.8 ^a	0.97
	II	14.50 \pm 2.23 ^a	15.76 \pm 3.61 ^a	15.19 \pm 2.74 ^a	13.48 \pm 2.18 ^a	14.52 \pm 2.91 ^a	13.73 \pm 2.43 ^a	0.99
Creatinine (mg/dl)	I	1.12 \pm 0.11 ^a	0.94 \pm 0.11 ^{ab}	0.87 \pm 0.13 ^{ab}	0.91 \pm 0.09 ^{ab}	0.73 \pm 0.08 ^b	0.86 \pm 0.06 ^{ab}	0.02*
	II	1.16 \pm 0.12 ^a	1.08 \pm 0.13 ^a	1.00 \pm 0.08 ^a	0.93 \pm 0.12 ^a	0.95 \pm 0.1 ^a	0.96 \pm 0.12 ^a	0.68

Means bearing different superscripts differ significantly within the group ($p < 0.05$)

* $P < 0.05$; ** $P < 0.01$

Results and Discussion

The mean \pm SE values of induction dose of thiopentone sodium (5.61 \pm 0.7 mg/kg) and propofol (2.62 \pm 0.29 mg/kg) were reduced from reference ranges after administration of dexmedetomidine and atropine sulphate as preanaesthetics in both the groups in present study. Decrease in dose of induction anaesthetic agents was due to potent dose sparing effect of dexmedetomidine as sedative agent. Similar observations were reported by Mate and Aher, (2019) [12] and Saini *et al.* (2019) [13] after administration of dexmedetomidine as preanaesthetic prior to induction with propofol and thiopentone sodium, respectively. The mean \pm SE values of recovery period were 8.17 \pm 0.79 minutes in group I and 7.33 \pm 1.71 minutes in group II, which differ non-significantly between the groups. Short recovery time was recorded in both the groups which might be due to lower blood gas partition coefficient of isoflurane.

Excellent sedation quality was found in all the dogs of both groups. Dexmedetomidine with atropine sulphate produced potent sedative effect in dogs in present study and similar finding was also recorded by Kuusela *et al.* (2001) [14]. Thiopentone sodium and propofol achieved excellent quality of induction with smooth, rapid and desire depth of induction anaesthesia in all the animals of both the groups. Similar findings were reported by Saini *et al.* (2019) [13] and Smith *et al.* (2017) [15]. In both the groups, quality of maintenance anaesthesia was found excellent with completely abolished jaw tone, pedal reflex and palpebral reflex along with ventromedial rotation of eyeball after induction of anaesthesia and during maintenance period. Recovery was smooth and uneventful without any complication in all the animals of both the groups.

Rectal temperature and respiratory rates decreased gradually and significantly after induction of anaesthesia upto end of observation period within both the groups. Dexmedetomidine contribute to hypothermia by activation of α -2 receptors and decreasing muscular activity (Lemke, 2007) [1]. Combined respiratory depression effects of dexmedetomidine and thiopentone sodium/propofol might result in decrease respiratory rates during study period (Sabbe *et al.*, 1994) [16]. Similar observation of decrease in rectal temperature and respiratory rates were reported by Jena *et al.* (2014) [17]; Saini *et al.* (2017) [7] and Mate and Aher (2019) [12]. As compared to baseline values (prior to preanaesthetic), pulse rate decreased significantly after induction of anaesthesia and thereafter decreased non-significantly till the end of observation period within both the groups. Initial decrease in pulse rate after administration of dexmedetomidine was due to reflex bradycardia as a result of α -2 agonist induced vasoconstriction (Lemke, 2007) [1]. Non-significant difference was observed in the mean values of systolic, diastolic and mean arterial blood pressure within groups at different time intervals. However, it increased non-significantly after

induction of anaesthesia as compared to base line values (prior to preanaesthetic) in both the groups. Similarly, Kuusela *et al.* (2001) [14]; Kojima *et al.* (2002) [18] and Villamandos *et al.* (2006) [6] also observed increase in blood pressure after administration of dexmedetomidine. Saturation of peripheral oxygen (SpO₂) showed non-significant difference within groups in both groups. All clinico-physiological parameters showed non-significant difference in between the groups.

There was gradual and significant decrease in mean values of haemoglobin, packed cell volume and total erythrocyte count at 15th, 30th, 45th and 60th minute intervals after induction of anaesthesia than baseline values (prior to preanaesthetic) within both the groups. Similar findings have been observed by Singh *et al.* (2013) [19] and Dewangan *et al.* (2016) [20]. Decrease in haemoglobin, packed cell volume and total erythrocyte counts might be due to pooling of blood cells in the spleen induced by adrenolytic property of α -2 agonist and haemodilution (Mazumdar *et al.*, 2015) [21]. Total leukocyte count showed gradual and significant decrease in group I and non-significant decrease in group II till the end of observation periods within the groups in both the groups. This decrease in leukocyte count may be due to enhanced peripheral blood level of adrenaline and nor-adrenaline which suppresses proliferative response of peripheral blood leucocytes (Felsner *et al.*, 1995) [22]. There was significant difference in differential leukocyte count in group I; while, non-significant difference was observed in group II. As compared to the baseline value (prior to preanaesthetic), mean values of blood glucose decreased non-significantly after induction and at 15th, 30th and 45th minute intervals; while, it increased non-significantly at 60th minute interval after induction of anaesthesia within groups in both the groups. All the haematological parameters showed non-significant difference in between the groups.

Gradual and non-significant decrease in mean values of total protein was observed upto 15th minute interval after induction of anaesthesia and thereafter significant decrease was observed till the end of observation period within both the groups. Similarly, Mazumdar *et al.* (2015) [21] and Saini *et al.* (2017) [7] also reported non-significant decrease in total protein. Alanine amino transferase (ALT) showed non-significant decrease till the end of observation period as compared to the base value (before preanaesthetic) within the group in both groups. Decrease in ALT level may be due to decreased hepatic blood flow because of reduced cardiac output influenced by anaesthetic effect that led to less production of liver enzyme (Thomson *et al.*, 1986) [23]. When compared to base value (prior to preanaesthetic), mean values of blood urea nitrogen were non-significantly increased after induction of anaesthesia and then non-significantly decreased till the end of observation periods in both the groups. Similar findings were observed by Jena *et al.* (2014) [17] and Saini *et*

al. (2017) [7] in their study. Blood urea nitrogen values decreased in present study might be due to continuous infusion of intravenous fluids that maintains the normal kidney function. Mean values of creatinine were non-significantly decreased than base line values (prior to preanaesthetics) at different time intervals in both the groups, except at 45th minute interval after induction of anaesthesia in group I. Similarly, Jena *et al.* (2014) [17] and Rafee *et al.* (2015) [24] reported non-significant decrease in creatinine values after administration of dexmedetomidine and propofol in dogs. However, in contrast to the present study, Saini *et al.* (2017) [7] reported significant increase in creatinine values upto 60th minutes. All serum biochemical parameters showed non-significant difference in between the groups.

Dexmedetomidine with atropine sulphate provided excellent quality of sedation and potent dose sparing effect on induction doses of thiopentone sodium and propofol in dogs. Both anaesthetic combinations provided smooth, rapid and excellent quality of induction along with smooth and rapid recovery without any complication in all the dogs. All clinico-physiological and haemato-biochemical parameters remained within normal physiological limits in both the groups.

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