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Comparison of haematological and haemodynamic alterations associated with lidocaine, bupivacaine, and ropivacaine epidural anaesthesia in dogs

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Abstract

Epidural anaesthesia is one among the most frequently used central neuraxial block techniques because of its simplicity and safety. This study aimed to assess the changes in haematological and haemodynamic parameters induced in dogs by epidurally administered lidocaine, bupivacaine, and ropivacaine together with dexmedetomidine in atropine-midazolam premedicated dogs subjected to elective ovariohysterectomy. A total of twenty-four adult dogs were allocated randomly (n=6) to 4 different groups, namely: A (dexmedetomidine), B (dexmedetomidine with lidocaine), C (dexmedetomidine with bupivacaine), and D (dexmedetomidine with ropivacaine). After a 10 minute premedication period, Dexmedetomidine @ 7 µg/kg, Lidocaine @ 4.4 mg/kg, Bupivacaine @ 2 mg/kg and Ropivacaine @ 2 mg/kg were dispensed into the epidural space. Different haematological and haemodynamic parameters were recorded during the study period. Haemoglobin levels showed a significant decline in Group B at the 30 and 90 minute with respect to baseline values. Packed cell volume, neutrophil and lymphocyte counts showed nonsignificant changes in all the groups relative to baseline. At 90 minutes, Group D exhibited a highly significant reduction ($p < 0.05$) in total leukocyte count compared to the other groups. Groups A, C and D exhibited significant variations in systolic, diastolic blood pressure, mean arterial pressure and haemoglobin oxygen saturation (S_pO_2) at various time points with respect to the baseline values. It was concluded that combining dexmedetomidine with lignocaine for epidural administration does not lead to haematological or haemodynamic instability.

1. Introduction

Epidural anaesthesia is recognized as one of the most effective analgesic procedures. Due to its simplicity and safety, it is one of the most common approach utilized for central neuraxial blockade. It offers effective intraoperative pain relief and enhances postoperative recovery (Brodner et al. 1999; Tomulic et al. 2023). Moreover, epidural anaesthesia is being used more frequently in high risk surgical procedures as well (Vaisanen et al. 1998) and in the management of critically ill animals (Jones 2000). Its advantages include more effective suppression of the surgical stress response and improved postoperative pain management. A variety of pharmacological agents commonly used for epidural anaesthesia include local anaesthetics (Freire et al. 2010; Odette and Smith 2013), morphine administered either alone or in combination with local anaesthetics or other sedatives (Carregaro et al. 2014) as well as α2 agonists (xylazine) and ketamine.

Lidocaine is one of the most frequently used agents for epidural anaesthesia; however, its use is associated with dose dependent side effects on the cardiovascular and central nervous system including hypotension and neurotoxicity (Beasley 1999). Concerns over the cardiotoxicity of bupivacaine eventually led to the development of ropivacaine, a safer, long- acting amino ethylamide local anaesthetic with reduced toxic potential. Dexmedetomidine, a powerful and highly selective α2 agonist has gained wide clinical adoption due to its sedative, analgesic, sympatholytic, and cardioprotective effects particularly lowered blood pressure and heart rate (Gertler et al. 2001). The individual drug doses and therefore the undesirable side effects may be reduced when two or more drugs are administered in combination providing a balanced epidural analgesia with lesser haemodynamic and haematological after effects (Sekhar et al. 2020). Therefore, the current study was taken to evaluate the haematological and haemodynamic variations induced by epidurally administered lidocaine, bupivacaine and ropivacaine in combination with dexmedetomidine in atropine-midazolam premedicated dogs undergoing elective ovariohysterectomy procedure.

2. Materials and Methods

Between October 2015 and May 2016, a total of 24 healthy, client owned, adult mixed breed dogs with an average body weight of 18.1 ± 2.4 kg were presented for elective ovariohysterectomy at the Division of Surgery, ICAR-Indian Veterinary Research Institute, Izatnagar, Uttar Pradesh, India. Food and water were restricted for 12 and 6 hours, respectively, prior to surgery. Written consent was acquired from the owners before proceeding with the surgical procedure. The 24 dogs were randomly assigned to four groups, with 6 animals in each group (n = 6) viz. A (dexmedetomidine), B (dexmedetomidine and lidocaine), C (dexmedetomidine and bupivacaine) and D (dexmedetomidine and ropivacaine).

After ensuring proper control and recording all baseline parameters, the animals were premeditated with atropine sulphate (0.5 mg/ml; Bhavani Pharmaceuticals Pvt. Ltd. India) inoculated intramuscularly at a dosage of 0.04 mg/kg body weight. Five minutes later, sedation was induced using an intravenous injection of midazolam (1 mg/ml; Neon Laboratories Ltd. India) at a dose of 0.7 mg/kg body weight. After achieving adequate sedation 10 minutes post midazolam administration, the dogs were positioned in sternal recumbency with their hind limbs positioned cranially. Epidural anaesthetic agents were then administered at the lumbosacral space (L7–S1) as per the following group protocols:

- Group A received Dexmedetomidine at 7 µg/kg (Dextomid 100 µg/ml, Neon Laboratories Ltd., India)
- Group B received Dexmedetomidine at 7 µg/kg + Lidocaine at 4.4 mg/kg (LOX 2%, Neon Laboratories Ltd., India)
- Group C received Dexmedetomidine at 7 µg/kg + Bupivacaine at 2 mg/kg (ANAWIN 0.5%, Neon Laboratories Ltd., India)
- Group D received Dexmedetomidine at 7 µg/kg + Ropivacaine at 2 mg/kg (ROPIN 0.75%, Neon Laboratories Ltd., India).

1% propofol (Nirfol 1%, Nirlife Limited, India) was administered in all the 4 groups intravenously as an intraoperative supplemental anaesthetic agent, whenever required during the procedure.

Blood samples (2.5 ml) were collected from each animal from the cephalic vein into heparinized vials at three time intervals: baseline (0 minutes), 30 minutes and 90 minutes following epidural drug administration. The haematological parameters analyzed were haemoglobin (Hb), packed cell volume (PCV), total leukocyte count (TLC), Neutrophil and lymphocyte count (%) as per Schalm et al. (1975). The haemodynamic parameters were recorded at the following time intervals: baseline (0 minutes), and subsequently at 5, 10, 20, 30, 45, 60, 75 and 90 minutes after the epidural administration of the drugs. The parameters recorded by a non- invasive approach, were systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP). The oxygen saturation of haemoglobin (SpO_2) was recorded using a pulse oximeter.

The data were first tested for normal distribution using the Shapiro-Wilk test. To compare mean values across different time points among the groups, Analysis of Variance (ANOVA) followed by Duncan's Multiple Range Test (DMRT) was applied. Within each group, changes over time were assessed using one-way repeated measures analysis, as described by Snedecor and Cochran (1994). Statistical analysis was performed using SPSS version 20.0 (IBM, IL, USA). Differences were considered statistically significant at p value < 0.05 and highly significant at p value < 0.01.

3. Results and Discussion

Haemoglobin levels have exhibited a nonsignificant reduction (P>0.05) from baseline in groups A, C and D across all observation periods. In contrast, a significant reduction (P<0.05) was noticed in group B at both 30 minute and 90 minute intervals. Packed cell volume (PCV) has decreased notably (P<0.05) at 30 minutes in groups A and B, and at 90 minutes time interval in group C. Group D exhibited no significant changes (P>0.05) throughout the study. Additionally, no remarkable differences (P>0.05) in PCV and haemoglobin values were found between the groups (Table 1). The decline in Hb and PCV can be linked to shifting of fluids from the extravascular space to intravascular space as a compensatory response to maintain cardiac output under anaesthesia during any surgical procedure (Wagner and Hitchcliff 1991; Lijima et al. 2013). Fluid therapy through intravenous route during the procedure leads to haemodilution which further might have decreased the Hb and PCV (Skarda and Muir 1994; Quispe-Cornejo et al. 2022). Earlier studies have has shown that epidural administration of xylazine can lead to a marked reduction in Hb and PCV, likely due to an increase in plasma volume resulting from vasodilation, which causes vascular pooling or sequestration of the blood cells in the spleen and lungs during anaesthesia (Skarda 1996; Papudesi et al. 2025). Similarly, subarachnoid injection of $\alpha 2$ agonists like xylazine and medetomidine has been associated with decreased Hb and PCV levels in goats (Kinjavdekar et al. 2000), and dogs (Amarpal et al. 1998). Further, the drop in Hb and PCV following epidural administration of ropivacaine has been documented in both healthy and uraemic goats (Singh et al. 2005).

Total leukocyte count (TLC) showed a significant reduction (P<0.05) at 90 minutes in groups B and D compared to their baseline levels. Notably, group D exhibited a highly significant decrease (P<0.01) at 90 min mark in comparison to the other groups (Table 1). This decline in TLC may be linked to the sequestration of circulating leukocytes in the spleen or other reservoirs, likely due to reduced sympathetic tone induced by epidural administration of local anaesthetics. Previous studies involving systemic $\alpha 2$ agonists have also reported a drop in TLC in dogs (Amarpal et al. 1998). Furthermore, a slight but statistically nonsignificant reduction in TLC following epidural xylazine administration was observed in dogs (Kelawala et al. 1996).

Neutrophil counts showed no significant changes (P>0.05) at any time point in any group compared to baseline values. Slight increase, though non-significant in neutrophil counts were observed, likely reflecting the anaesthetic and surgical stress - induced glucocorticoid release, stimulating neutrophil mobilization (Ivascu et al. 2024). A similar rise in neutrophil levels was noted in buffalo calves following administration of xylazine and lidocaine (Singh et al. 2005). Conversely, slight decreases seen in groups B, C and D at various intervals may result from a blunted stress response either by dexmedetomidine with local anaesthetics or indirectly by sedation and analgesia. Reduced neutrophil counts have also been reported in dogs treated with $\alpha 2$ agonists (Amarpal et al. 1998). Lymphocyte counts in groups A and D appeared to inversely correlate with neutrophil levels, declining whenever neutrophils increased (Table 1). Systolic blood pressure (SBP) (Fig. 1a), diastolic blood pressure (DBP) (Fig. 1b) and mean arterial

Table 1. Mean ± SD values of hematological parameters in different groups at different time intervals

Parameter	Group	Time interval (min)		
		0	30	90
[a]Hb (g/dl)	A	110.2±12.89	101.6±5.22	98.6±5.46
	B	119.2±18.47	113±16.58*	100.4±20.07*
	C	114.4±15.06	101.6±22.24	103.6±26.13
	D	120.8±12.93	118.8±12.38	113.4±6.39
[b]PCV	A	0.44±0.05	0.39±0.05*	0.36±0.08
	B	0.46±0.04	0.42±0.06*	0.40±0.07
	C	0.44±0.04	0.38±0.07	0.38±0.07*
	D	0.47±0.03	0.46±0.02	0.44±0.04
[c]TLC (× 10^9/L)	A	7.5±1.61	6.8±2.03	6.41±1.59^{B}
	B	9.8±2.18	10.8±3.95	7.42±1.68*^{B}
	C	8.45±3.49	7.99±3.89	6.44±1.33^{B}
	D	8.26±1.58	7.28±1.57	3.91±1.76**^{A}
Neutrophils (%)	A	64.2±8.53	66±8.37	64.6±5.81
	B	62.4±10.14	57.6±13.65	66.8±10.01
	C	62.8±6.61	63.4±5.27	61±6.08
	D	62.4±10.71	65.4±6.54	58.2±9.96
Lymphocytes (%)	A	28±5.87	26.4±7.13	30.8±5.54
	B	30.4±9.81	26±11.02	28±7.48
	C	26.4±3.36	29±5.79	29±5.34
	D	30±10.68	26.2±3.9	34.4±11.61

[a] Hemoglobin, [b] Packed cell volume, and [c] Total leucocyte count
Values with Superscripts A and B among groups represent significant difference (p<0.05) at corresponding intervals. *Significantly different from base value (p<0.05) and **Very significantly different from base value (p<0.01)

pressure (MAP) (Fig. 1c) initially rose in all groups, followed by a gradual decline relative to baseline values over the course of the study.

Local anaesthetics produce a non-selective blockade of sensory, sympathetic and motor nerve fibers. The resulting sympathetic block leads to vasodilation in the anaesthetized regions, which can cause dose - dependent hypotension, a frequently observed cardiovascular complication in animals (Torske and Dyson 2000). However, in the current study, the epidural co-administration of dexmedetomidine with local anaesthetics in groups B, C and D, along with the systemic administration of atropine across all groups might have counteracted the hypotensive effects of local anaesthetics. α-2 agonists are known to cause a biphasic cardiovascular response - initially inducing peripheral vasoconstriction with elevated blood pressure, followed by reduced sympathetic outflow and blood pressure. A similar pattern was observed in the current study. Anticholinergic agents like atropine and glycopyrrolate have been incriminated to cause tachycardia and hypertension in dogs (Alibhai et al. 1996). The decline in blood pressure following the initial increase may be attributed to the metabolism and systemic clearance of dexmedetomidine and atropine. Additionally, midazolam may have promoted to drop in blood pressure, as it is known to exert minimal effects on cardiac function but has been associated with significant reductions in arterial pressure in dogs (Butola and Singh 2007). Furthermore, the use of supplemental propofol during surgery in the present study may have further given rise to the reduction in blood pressure. When Propofol is used for induction as well as for maintenance of anaesthesia, it lowers the systemic blood pressure, primarily due to peripheral vasodilation, cardiovascular depression and reduced cardiac output (Coates et al. 1987; Claeys et al. 1988; Sebel and Lowdon 1989).

In terms of systolic blood pressure (SBP), groups A, B and C showed statistically nonsignificant changes (P>0.05) relative to their baseline values, while group D exhibited an initial significant increase (P<0.05). Animals in group C demonstrated a significant decrease (P<0.05) in SBP in comparison to the other groups at various intervals (Fig. 1a). This decline in SBP in group C may be linked to reduced myocardial contractility due to suppression of baroreceptor reflexes and

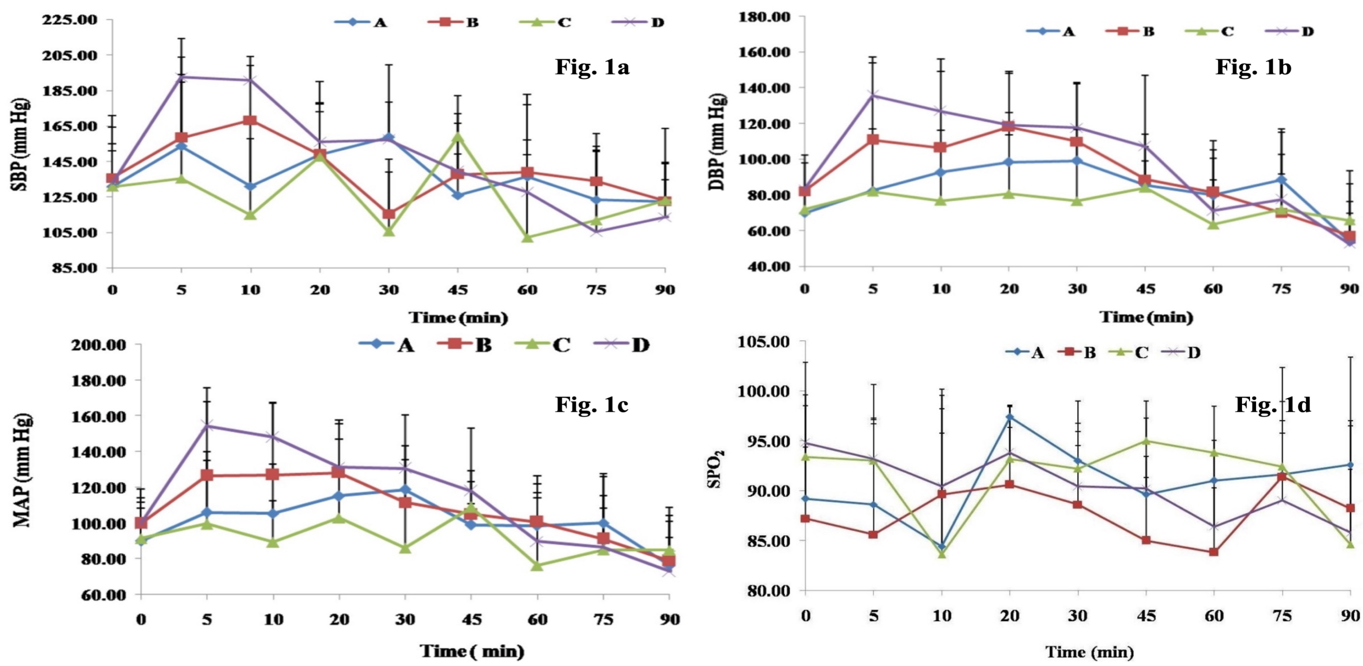

Fig. 1. *Mean ± SD values of (a) Systolic blood pressure (mm Hg), (b) Diasystolic blood pressure, (c) Mean arterial pressure (mm Hg), and (d) SpO_2 (%) in different groups at different time intervals*

drop in catecholamines due to sympathetic blockade of the adrenal medulla by bupivacaine (Watanabe et al. 1995). Similar findings have been observed where epidural administration of medetomidine in association with ketamine or bupivacaine significantly lowered SBP (Singh et al. 2005). Regarding diastolic blood pressure (DBP) and mean arterial pressure (MAP), both parameters showed a significant increase ($P<0.05$) initially in groups A and D. However, group A later exhibited a non-significant decline ($P>0.05$), whereas group D showed a significant decrease ($P<0.05$) that persisted until the end of the study (Fig. 1b; Fig. 1c). This decline in DBP and MAP is in alignment with the findings of previous studies (Hurley et al. 1991; Duke et al. 2000; Eryilmaz and Günaydin 2011). However, the decrease in group D during the course of study was within clinically acceptable limits.

Mild nonsignificant reduction ($P>0.05$) in peripheral oxygen saturation (SpO_2) was observed across all groups compared to baseline values. However, group B animals showed a significantly lower SpO_2 ($P<0.05$) than those in group C at the 45 and 60 minute time intervals (Fig. 1d). The mild non- significant decrease in SpO_2 seen in all groups of dogs may be incriminated to the sedative effects of propofol, which can lead to decreased inspired oxygen levels, hypoventilation, ventilation-perfusion mismatch, diffusion limitations and intrapulmonary shunting (Quandt et al. 1998). Moreover, $\alpha2$ agonists have been linked to reduce arterial oxygen partial pressure (PaO_2) in domestic and wild ruminants (Read et al. 2003) and sheep (Kastner 2006) leading to hypoxemia. In a study conducted by Salve et al. (2022) marked reduction in oxygen saturation values under xylazine and tiletamine-zolazepam anaesthesia in dogs has been reported and this can be attributed to lowered respiratory depth due to alpha-adrenergic agonistic action of xylazine. Midazolam has also been linked to lowered SpO_2 levels (Butola and Singh 2007). Similar to the present findings, previous investigations have too reported decreased SpO_2 following the epidural administration of lidocaine in cats, which supports the significant drop observed in animals belonging to group B in comparison to group C at various intervals (DeRossi et al. 2009).

4. Conclusion

Epidural administration of dexmedetomidine with local anaesthetics in atropine- midozolam premedicated dogs does not cause haematological instability and appears safe for elective ovariohysterectomy procedure. However, significant alterations in blood pressure in groups with dexmedetomidine-bupivacaine and dexmedetomidine-ropivacaine are suggestive of the need for better intraoperative monitoring and subsequent measures in cases of any urgency. Among the combinations studied, dexmedetomidine - lignocaine may be considered better than the combination of dexmedetomidine with bupivacaine or ropivacaine as far as haemodynamic stability is concerned.

Declarations

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Conflict of interest: None to declare

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Ethical approval: As the laboratory animal experiments were not performed in the present research work so, informed consent was acquired from clients of the dogs prior to initiating the elective ovariohysterectomy procedure.

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