



RESEARCH ARTICLE

The Hematological and Cardiopulmonary Effects of Epidural Xylazine, Lidocaine and Their Combination in Acepromazine Sedated Dogs

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ABSTRACT

A study was carried out to compare the effects of epidural xylazine, lidocaine and their combination on hematological and cardiopulmonary parameters in dogs. Fifteen healthy dogs were used in this study. The dogs were randomly assigned to three groups of five animals each. The first group was injected with 2% lidocaine hydrochloride at 4 mg/kg body weight, the second with 2% xylazine hydrochloride at 0.6 mg/kg body weight while the third group was injected with the drug combination of lidocaine and xylazine at 2 and 0.3 mg/kg respectively, in the same syringe. All injections were made into the lumbosacral space. Changes in cardio-pulmonary and hematological parameters in dogs were recorded over a 4-hour monitoring period.

Epidural administration of lidocaine and xylazine resulted in significant ($P<0.05$) decline in TEC, PCV and Hb. Significant ($P<0.05$) changes in heart rate occurred only in dogs administered with epidural xylazine and the drug combination of lidocaine-xylazine. Dogs injected with epidural lidocaine, xylazine and lidocaine-xylazine had significant ($P<0.05$) changes in their respiratory rates. Lumbosacral injection of lidocaine-xylazine combination resulted in a significant ($P<0.05$) bradycardia and respiratory depression compared to the individual drugs.

It is concluded that significant cardiopulmonary depression should be anticipated particularly when lidocaine-xylazine and xylazine are used for epidural anaesthesia in dogs. Devoted monitoring is therefore imperative to avoid untoward outcomes.

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INTRODUCTION

Epidural regional anaesthesia is a technique used in small and large animals, and is indicated for surgical procedures caudal to the umbilicus (Skarda, 1996).

Local anaesthetic drugs and alpha-2 adrenoceptor agonists have been used to produce epidural anaesthesia in dogs (Greene *et al.*, 1995; Rector *et al.*, 1998; Adentunji *et al.*, 2001). The most popular local anaesthetic drug used to produce epidural anaesthesia in dogs is lidocaine (Skarda, 1996). Local anesthetic agents indiscriminately block motor, sensory, and sympathetic fibers causing ataxia, analgesia, hypothermia and cardiopulmonary depression (Day and Skarda, 1991). Some studies carried out in dogs have shown that epidural administration of lidocaine has no significant changes on heart rate, mean arterial pressure, respiratory rate and

temperature (Adetunji *et al.*, 2001; Vnuk *et al.*, 2006). However, no study has evaluated the hematological effects of epidural lidocaine in dogs.

On the other hand xylazine, an alpha-2 adrenoceptor agonist exhibits sensory and motor nerve blocking actions in addition to its spinal cord alpha-2 adrenoceptor mediated analgesic effects (Skarda, 1996). Significant depression of cardiopulmonary function has been reported following epidural xylazine in dogs (Rector *et al.*, 1998; Mohammad, 2003; Soares *et al.*, 2004). Similar results have been reported in cats (Adentunji *et al.*, 2002), cattle (Skarda *et al.*, 1990; Jean *et al.*, 1990; Nowrouzian *et al.*, 1991) and goats (DeRossi *et al.*, 2005) after epidural xylazine injection. Decrease in total leucocytes count, packed cell volume and hemoglobin concentration following epidural administration of xylazine have also been observed previously in dogs (Farheen *et al.*, 2008),

cattle (Jean *et al.*, 1990) and horses (Skarda and Muir, 1996).

In recent years, lidocaine and xylazine combination has been used in dogs because of the resulting synergistic antinociceptive effects. However, the effects of lidocaine-xylazine combination on hematological and cardiopulmonary functions have not been explored in dogs. This study therefore reports on the effects of epidural lidocaine, xylazine and their combination on hematological and cardiopulmonary parameters at recommended dosages in dogs.

MATERIALS AND METHODS

Fifteen healthy mongrel dogs, comprising males and females aged 3-5 years were used for the study. Only intact male and intact, non-pregnant female dogs were used. Dogs were housed individually in kennels and provided food once per day. Water was provided ad libitum.

The fifteen dogs were randomly divided into three treatment groups of five dogs each. The first treatment involved lumbosacral epidural administration of lidocaine (Lidocaine injection B.P 2%, Macs Pharmaceuticals Ltd, Nairobi, Kenya) at a dosage of 4 mg/kg. The second treatment involved lumbosacral epidural administration of xylazine (Agrar, Agrar Holland BV, Scest Holland) at a dosage of 0.6 mg/kg. The third treatment involved lumbosacral epidural administration of lidocaine-xylazine mixture at half the dosage of each individual drug (lidocaine at 2 mg/kg and xylazine at 0.3 mg/kg).

Food and water was withheld from the dogs on the morning of the trials. Dogs were sedated 30 minutes before administration of epidural drugs using acepromazine (Aceprom Inj, Centaur Labs, Isando) at 0.1 mg/kg intramuscular injection in the gluteus muscles. The lumbosacral region was shaved and prepared for aseptic injection. An assistant restrained the dog in sternal recumbency on a table, with its pelvic limbs extended cranially to maximally separate the lumbar vertebrae. The lumbosacral (L7-S1) space was then located as described by Skarda, (1996). The injection site was infiltrated subcutaneously with 1.0 ml of 2% lignocaine hydrochloride to minimize the pain of epidural puncture in an awake but sedated dog.

A 21 gauge hypodermic needle was inserted percutaneously at the prepared site into the epidural space. After confirming correct needle placement, all injections were made over a period of 20 seconds. Where the volume of the drug to be injected varied between dogs in each group, a standard volume was ensured by adding sterile saline solution to make the difference in calculated volume of drug. The treated dog was supported in sternal recumbency for 3 minutes following drug injection to achieve a bilateral rather than unilateral blockade.

An intravenous catheter was placed in the cephalic vein of each acepromazine sedated dog. About 0.5ml of EDTA blood was collected from each dog through the catheter at 0 minutes, which is before administration of the epidural drugs and then at 15, 30, 60, 120, 180 and 240 minutes after the administration of the epidural drugs. The blood samples were evaluated for Hemoglobin concentration (Hb) in g/dl, Packed Cell Volume (PCV) in

%, Total Leukocyte Count (TLC) in millions/mm³, Total Erythrocyte Count (TEC) in millions/mm³, and Total Platelet Count (TPC) in millions/mm³ using an automated cell counter (MS4 VET hematology machine, Melet Schloesing pharmaceuticals SA, Suisse, Switzerland) following the manufacturer's instructions.

Heart rate (HR) and Respiratory rate (RR) were taken at 5 minutes before epidural drug injection, which was designated as baseline and taken as 0 minutes and then at 5, 10, 15, 30, 45, 60, 75, 90, 120, 150, 180, 210 and 240 minutes after epidural drug injection.

Data analysis

Data was expressed as means (\pm SD) of the 5 dogs. The measured cardiopulmonary variables were compared using ANOVA for repeated measures. Where a significant difference was indicated by ANOVA, least significant difference (LSD) test was employed as post-test. P value of <0.05 was accepted as being significant in all comparisons.

RESULTS

Hematology

Epidural administration of lidocaine and xylazine resulted in significant decline only in TEC, PCV and Hb. However, epidural lidocaine-xylazine combination did not have any significant changes on hematological parameters.

The TEC values in dogs injected with epidural xylazine decreased significantly ($P<0.05$) post-drug injection, being 4.57 ± 0.43 million/mm³ at 120 minutes and declining further to 4.27 ± 0.62 million/mm³ at 240 minutes from baseline values of 5.03 ± 0.64 million/mm³. In dogs injected with epidural lidocaine, apart from decreasing of TEC values being significant ($P<0.05$), they started decreasing notably earlier post-drug injection compared to the other two groups. The TEC values in this group declined steadily through most time intervals of evaluation, being 4.56 ± 0.21 million/mm³ as early as 15 minutes post-drug injection to 4.37 ± 0.30 million/mm³, 4.32 ± 0.16 million/mm³, 4.38 ± 0.27 million/mm³ at 60, 180 and 240 minutes respectively from baseline values of 4.86 ± 0.26 million/mm³.

In these two groups of individual epidural drug injections, the TEC had not returned to baseline values at the end of the 4 hour evaluation period.

In the groups of dogs where epidural xylazine and lidocaine were administered, the PCV values significantly decreased below baseline values. In the dogs injected with epidural xylazine, there was a statistically significant ($P<0.05$) decline in PCV values being $29.64\pm 4.0\%$ at 180 minutes and $28.56\pm 4.91\%$ at 240 minutes post-drug injection respectively, from the baseline value. PCV values remained significantly ($P<0.05$) lower than the baseline value even at the end of the 4 hour evaluation period (Table 1).

Dogs with epidural injection of lidocaine were found to have significantly ($P<0.05$) lower PCV values of $30.72\pm 5.09\%$ at 15 minutes and $29.66\pm 4.55\%$ at 30 minutes post-drug injection, respectively from baseline values.

Table 1: Means (\pm SD; n=5) of hematological parameters of dogs under epidural anaesthesia with lidocaine, ketamine, xylazine, lidocaine-xylazine, lidocaine-ketamine and xylazine-ketamine

Groups	Time (Minutes)	TLC (Millions/mm ³)	TEC (Millions/mm ³)	TPC (Millions/mm ³)	PCV (%)	HB (g/dl)
Xylazine	0	11438 \pm 3041.31	5.03 \pm 0.64	134.2 \pm 42.23	34.40 \pm 5.98	13.40 \pm 2.46
	15	12304 \pm 4054.80	4.72 \pm 0.34	134.0 \pm 43.70	32.54 \pm 2.71	12.58 \pm 1.54
	30	12728 \pm 4140.79	4.69 \pm 0.24	143.8 \pm 42.94	31.82 \pm 2.84	12.52 \pm 1.38
	60	11840 \pm 2898.23	4.65 \pm 0.16	122.0 \pm 25.64	31.48 \pm 1.80	12.36 \pm 1.16
	120	12616 \pm 2679.35	4.57 \pm 0.43 *	126.8 \pm 38.78	30.72 \pm 3.90	12.24 \pm 1.47
	180	11158 \pm 2158.63	4.39 \pm 0.40 *	132.4 \pm 53.95	29.64 \pm 4.00 *	11.74 \pm 1.51 *
	240	11528 \pm 2587.30	4.27 \pm 0.62 *	135.4 \pm 62.44	28.56 \pm 4.91 *	11.26 \pm 2.05 *
Lidocaine	0	11120 \pm 3533.92	4.86 \pm 0.26	134.4 \pm 41.63	33.06 \pm 6.05	12.68 \pm 2.03
	15	11146 \pm 1809.08	4.56 \pm 0.21 *	124.4 \pm 59.41	30.72 \pm 5.09 *	11.80 \pm 1.68
	30	11836 \pm 3043.32	4.39 \pm 0.24 *	111.6 \pm 35.66	29.66 \pm 4.55 *	11.38 \pm 1.73 *
	60	12736 \pm 3207.35	4.37 \pm 0.30 *	111.4 \pm 43.71	29.50 \pm 3.10	11.30 \pm 1.20 *
	120	14555 \pm 4762.71	4.36 \pm 0.29	133.8 \pm 27.86	28.50 \pm 3.40	10.73 \pm 1.24
	180	14292 \pm 4319.82	4.32 \pm 0.16 *	137.2 \pm 32.00	29.20 \pm 3.51	11.42 \pm 1.33
	240	13288 \pm 3750.48	4.38 \pm 0.27 *	128.2 \pm 39.39	29.24 \pm 3.65	10.96 \pm 1.26
Lidocaine-xylazine	0	10794 \pm 3393.40	4.83 \pm 0.42	103.0 \pm 34.23	31.08 \pm 4.70	12.22 \pm 1.70
	15	11162 \pm 3901.38	4.77 \pm 0.58	113.6 \pm 35.15	30.36 \pm 4.07	11.74 \pm 1.33
	30	12014 \pm 4999.28	4.71 \pm 0.29	102.0 \pm 25.75	29.92 \pm 3.67	11.72 \pm 1.03
	60	11784 \pm 3564.29	4.74 \pm 0.66	102.4 \pm 27.23	30.32 \pm 4.17	11.78 \pm 1.39
	120	11224 \pm 2993.62	4.96 \pm 0.79	85.4 \pm 35.35	31.60 \pm 3.64	12.10 \pm 1.65
	180	11283 \pm 5094.02	4.82 \pm 0.85	78.8 \pm 40.62	31.00 \pm 3.75	11.90 \pm 1.69
	240	12562 \pm 5835.56	4.55 \pm 0.75	94.4 \pm 30.61	29.10 \pm 2.78	11.28 \pm 1.34

*Indicates mean value that differs significantly ($P < 0.05$) from baseline value; **Key:** TLC-Total leucocyte count; TEC-Total erythrocyte count; TPC-Total platelet count; PCV-Packed cell volume; Hb-Hemoglobin concentration

Generally, for all the three treatment groups, the values of Hb concentration declined below baseline values and remained at those levels even by the end of the 4 hour evaluation period. The trends of Hb concentrations observed are summarized in Table 1.

Dogs injected with epidural xylazine had significantly ($P < 0.05$) lower hemoglobin concentration, which was 11.74 \pm 1.51 g/dl at 180 minutes post-injection and 11.26 \pm 2.05 g/dl at 240 minutes, from a baseline value of 13.40 \pm 2.46 g/dl. Similar results were recorded for dogs injected with epidural lidocaine with values of 11.38 \pm 1.73 g/dl and 11.3 \pm 1.2 g/dl at 30 and 60 minutes post-drug injection, respectively.

Cardio-pulmonary parameters

Heart rate

The heart rates (beats/minute) of the dogs in the three treatment groups are presented in Table 2 and illustrated in Figure 1. A sudden drop in heart rate was observed in dogs injected with epidural xylazine and lidocaine-xylazine 5 minutes post-drug injection. Heart rate in these two groups remained low up to 45 minutes post-drug injection when a steady increase in heart rate was observed until the end of the 4 hour monitoring period.

Significant changes in heart rate only occurred in dogs administered with epidural xylazine and drug combinations of lidocaine-xylazine. The heart rate of dogs injected with epidural xylazine significantly ($P < 0.05$) decreased to 65.6 \pm 12.20 beats/minute at 5 minutes post-drug injection and continued with a slight decline to 65 \pm 14.59 beats/minute at 75 minutes from a baseline value of 106.4 \pm 13.74 beats/minute. Thereafter, an up and down pattern in heart rate was observed up to the end of the monitoring period. However, these changes were not significant.

Significant ($P < 0.05$) decrease in heart rate was recorded from 57.1 \pm 4.59 beats/minute at 5 minutes to

57.6 \pm 18.02 beats/minute at 45 minutes in dogs injected with epidural lidocaine-xylazine combination compared to a baseline value of 92.0 \pm 28.71 beats/minute (Table 2).

The lowest heart rate recorded was for dogs injected with epidural xylazine, which was 50.4 \pm 9.21 beats/minute at 15 minutes post-drug injection, at what time the heart rate had declined to 47% of the baseline value (106.4 \pm 13.74 beats/minute). Epidural lidocaine-xylazine combination produced significant ($P < 0.05$) bradycardia in dogs when compared to xylazine or lidocaine injected alone.

There was no significant change in heart rate recorded after epidural injection of lidocaine. Heart rate in all the three groups of dogs returned to baseline values or at least approached those values by the end of the 4 hour monitoring period.

Respiratory rate

The respiratory rates (breaths/minute) of dogs in the three treatment groups are given in Table 3 and illustrated in Figure 2. Dogs injected with epidural lidocaine, xylazine and lidocaine-xylazine had significant changes in their respiratory rates. Dogs injected with lidocaine had significantly ($P < 0.05$) lower respiratory rate (12.0 \pm 0.0 breaths/minute) at 210 minutes post-drug injection as compared to baseline value (12.8 \pm 4.38 breaths/minute). Similar effects were observed in the dogs injected with epidural xylazine at 30 minutes (9.6 \pm 2.19 breaths/minute) through to 45 minutes (8.8 \pm 4.38 breaths/minute) post-drug injection.

Respiratory rate in dogs injected with lidocaine-xylazine was significantly ($P < 0.05$) lowered to 10.4 \pm 2.19 breaths/minute at 5 minutes post-injection and 9.0 \pm 3.0 breaths/minute at 15 minutes compared to a baseline value of 13.6 \pm 2.19 breaths/minute. Respiratory rate at 90 minutes post-drug injection remained significantly ($P < 0.05$) low (11.2 \pm 1.79 breaths/minute) through to 150

Table 2: Means (\pm SD; n=5) of heart rate (beats/minute) following epidural administration of lidocaine, xylazine and lidocaine-xylazine in dogs.

Time (Minutes)	Lidocaine	Xylazine	Lidocaine-xylazine
0	87.2 \pm 20.67	106.4 \pm 13.74	92.0 \pm 28.71
5	78.4 \pm 17.57	65.6 \pm 12.20*	57.6 \pm 14.59*
10	78.4 \pm 18.89	52.8 \pm 7.16*	56.8 \pm 13.08*
15	83.2 \pm 21.98	50.4 \pm 9.21*	52.0 \pm 11.66*
30	83.6 \pm 14.45	52.0 \pm 10.95*	55.2 \pm 15.59*
45	81.2 \pm 17.98	56.8 \pm 13.08*	57.6 \pm 18.02*
60	85.6 \pm 15.39	58.4 \pm 17.80*	71.2 \pm 26.44
75	81.6 \pm 21.84	65.5 \pm 14.59*	72.8 \pm 25.20
90	88.0 \pm 26.83	86.4 \pm 25.39	76.8 \pm 18.42
120	80.0 \pm 21.91	85.6 \pm 24.10	69.6 \pm 22.02
150	92.8 \pm 31.92	91.2 \pm 17.53	76.0 \pm 18.11
180	94.4 \pm 27.22	89.6 \pm 27.36	90.4 \pm 28.37
210	82.4 \pm 25.71	90.4 \pm 15.65	91.2 \pm 30.25
240	81.6 \pm 19.72	88.0 \pm 22.45	92.0 \pm 34.64

*Indicates mean value that differs significantly ($P < 0.05$) from baseline value.

Table 3: Means (\pm SD; n=5) of respiratory rate (breaths/minute) following epidural injection of lidocaine, xylazine and lidocaine-xylazine in dogs

Time (Minutes)	Lidocaine	Xylazine	Lidocaine-xylazine
0	12.8 \pm 4.38	14.4 \pm 2.19	13.6 \pm 2.19
5	10.4 \pm 2.19	11.2 \pm 3.35	10.4 \pm 2.19*
10	11.2 \pm 1.79	13.6 \pm 4.56	11.4 \pm 3.97
15	11.2 \pm 1.79	11.2 \pm 3.35	9.0 \pm 3.00 *
30	11.2 \pm 1.79	9.6 \pm 2.19*	11.2 \pm 3.35
45	10.4 \pm 2.19	8.8 \pm 4.38*	10.4 \pm 4.56
60	10.8 \pm 1.79	10.4 \pm 3.58	11.2 \pm 3.35
75	10.8 \pm 1.79	11.2 \pm 3.35	12.0 \pm 2.83
90	12.0 \pm 2.83	12.8 \pm 4.38	11.2 \pm 1.79*
120	12.8 \pm 1.79	13.6 \pm 3.58	11.2 \pm 1.79*
150	13.6 \pm 2.19	15.2 \pm 3.35	12.0 \pm 0.00*
180	13.6 \pm 2.19	16.0 \pm 2.83	12.8 \pm 1.79
210	12.0 \pm 0.00*	16.0 \pm 2.83	13.6 \pm 2.19
240	12.8 \pm 1.79	16.0 \pm 2.83	13.6 \pm 2.19

*Indicates mean value that differs significantly ($P < 0.05$) from baseline value.

minutes (12.0 \pm 0.0 breaths/minute), but had started to rise again towards the baseline value (13.6 \pm 2.19 breaths/minute).

Injection of the lidocaine-xylazine combination resulted in more severe depression of respiration when compared with lidocaine and xylazine alone. By the end of the 4 hour monitoring period, respiratory rate had returned to baseline values in all the three groups.

DISCUSSION

The results of the current study revealed that after epidural administration of lidocaine and xylazine there was generally a significant decrease in values of hematological parameters particularly total erythrocyte count (TEC), packed cell volume (PCV) and hemoglobin (Hb) concentration. Decrease in TEC, PCV and Hb following epidural administration of xylazine have also been observed previously in dogs (Farheen *et al.*, 2008), cattle (Jean *et al.*, 1990) and horses (Skarda and Muir, 1996). Similar findings have been reported following epidural xylazine-ketamine combination in buffalo calves (Singh *et al.*, 2006) and xylazine-ketamine combination in goats (Singh *et al.*, 2007). Pooling of circulating blood cells in the spleen and other reservoirs secondary to

decreased sympathetic activity that occurs during epidural anaesthesia, could be the reason for decrease in TEC, PCV and hemoglobin concentration (Macdonald and Virtanen, 1992). The fact that there is no decline in values of hematological parameters in splenectomized sheep (Hawkey, 1985), suggests that the spleen may be the main reservoir for these cells. The decrease in PCV and hemoglobin concentration can also be attributed to the shifting of fluid from extravascular compartment to intravascular compartment (Wagner *et al.*, 1991) in order to maintain normal cardiac output in the animals.

The observation of a moderate decrease in heart rate in the dogs injected with epidural lidocaine in the current study has similarly been found in previous studies on the cardiovascular effects of epidural block with lidocaine (Adetunji *et al.*, 2001; Vnuk *et al.*, 2006). These findings may be attributed to the fact that at high volumes, epidural lidocaine extends cranially into the thoracic region and blocks the sympathetic nerve fibers leading to bradycardia (Torske and Dyson, 2000). Moreover, lidocaine affects the sympathetic nerves leading to vasodilation of the dural blood vessels consequently causing reduced arterial blood pressure and subsequent bradycardia (Skarda, 1996).

A significant decrease in heart rate observed following epidural administration of xylazine in dogs in the current study is in agreement with similar decrease reported previously with the same drug in cattle (Jean *et al.*, 1990), sheep (Waterman *et al.*, 1987), mares (Skarda and Muir, 1996) and goats (Aithal *et al.*, 1996; Kinjavdekar *et al.*, 2000). A drop in heart rate is considered a classical response following systemic administration of alpha-2 adrenoceptor agonists (Ruffolo *et al.*, 1993). The bradycardia recorded after epidural administration of xylazine could be attributed to decreased sympathetic outflow from the central nervous system, inhibition of norepinephrine release from sympathetic nerve terminals, direct depression of cardiac pacemaker and conduction tissue, increased vagal tone and a direct increase in the release of acetylcholine from parasympathetic nerves in the heart (Macdonald and Virtanen, 1992).

The combination of lidocaine-xylazine resulted in slightly more pronounced bradycardia compared to xylazine alone. This decrease in heart rate in lidocaine-xylazine group might be due to summation of the depressant effects of the two drugs (Mpanduji *et al.*, 1999).

In the current study, significant respiratory depression produced by epidural xylazine in dogs has similarly been reported in dogs (Mohammad, 2003), cattle (Skarda and Muir, 1982a) and horses (Skarda and Muir, 1982b). All alpha-2 adrenoceptor agonists have been reported to cause some degree of respiratory depression. This effect might be attributed to the direct depression of the respiratory center through stimulation of supraspinal adrenoceptors following systemic absorption of the drug, as suggested previously (Lin-Huichu *et al.*, 1998; Prado *et al.*, 1999).

The lidocaine-xylazine combination resulted in slightly more depression of respiration in dogs compared to lidocaine and xylazine alone. These findings are in agreement with those reported in goats (Mpanduji *et al.*, 1999) and might be attributed to the synergism in the depressant effects of the two drugs on respiratory rate

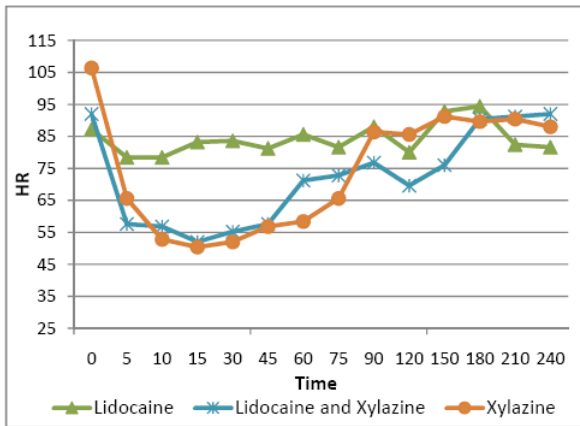


Fig. 1: Changes in mean heart rate values (beats/minute) following epidural administration of lidocaine, xylazine and lidocaine-xylazine in dogs.

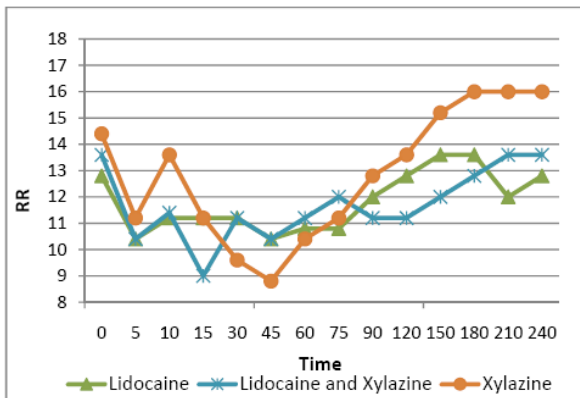


Fig. 2: Changes in mean respiratory rate (breaths/minute) following epidural injection of lidocaine, xylazine and lidocaine-xylazine in dogs

(Mpanduji *et al.*, 1999). Although administration of individual epidural drugs and drug combinations produced notable significant changes in cardiopulmonary function, the dogs nevertheless recovered from these effects without any undesirable effects.

Conclusion

Epidural administration of lidocaine, xylazine and lidocaine-xylazine combination in dogs causes non-harmful changes in hematological values.

Although depression of heart rate and respiratory rate induced by epidural administration of xylazine and lidocaine-xylazine drug combinations did not produce any harmful effects, careful monitoring of patients is pertinent to detect any early signs of impending undesirable outcomes.

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