Effects of epidural xylazine, lidocaine and their combination on body temperature in acepromazine-sedated dogs

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SUMMARY

A prospective randomized and blinded study was carried out to compare the effects of epidural xylazine, lidocaine and their combination on body temperature 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 at 4 mg/kg body weight, the second with 2% xylazine at 0.6 mg/kg body weight while the third group was injected with the drug combination of lidocaine and xylazine at 2 mg/kg body weight and 0.3 mg/kg body weight, respectively, in the same syringe. All injections were made into the lumbosacral space. Changes in rectal temperature were recorded over a 4-hour monitoring period. A significant ($p<0.05$) decline in the mean rectal temperature was observed in all three groups. Lidocaine caused a decrease in mean rectal temperature of 1.0 °C, xylazine 1.6 °C and lidocaine-xylazine 2.0 °C. At the end of the 4- hour monitoring period, the mean rectal temperature of the dogs in the lidocaine group remained significantly lower as compared to baseline values. Dogs injected with lidocaine had significantly higher mean temperature when compared to dogs injected with xylazine ($p=0.02$) and lidocaine-xylazine ($p=0.003$). Shivering was observed in 20% of the dogs in lidocaine group, 60% in xylazine group and 80% in lidocaine-xylazine group. It was concluded that epidural xylazine, lidocaine, and their combination caused significant change in mean rectal temperature even in the absence of any surgery. In clinical setting, this has both morbidity and mortality implications in the post-operative period.

Keywords: Dogs, Epidural, Lidocaine, Xylazine, Temperature

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 (Green *et al.,* 1995; Rector *et al.,* 1998; Adetunji *et al.,* 2001). The most popular local anaesthetic drug used to produce epidural anaesthesia in dogs is lidocaine (Skarda, 1996). Local anaesthetic agents indiscriminately block motor, sensory, and sympathetic fibers causing ataxia, analgesia, temperature and cardiopulmonary depression (Day and Skarda 1991). Some studies carried out in dogs have shown that epidural lidocaine has no effect on body temperature (Adentuji *et al.,* 2001; Vnuk *et al.,* 2006). However other authors have reported hypothermia following epidural lidocaine in other species like cats (De Rossi *et al.,* 2009) and goats (Mpanduji *et al.,* 1999).

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). Hypothermia has been reported in dogs when xylazine was administered epidurally (Mohammad, 2003; Soares *et al.,* 2004). Similar results have been reported in cats

(Adentuji *et al.,* 2002), cattle (Skarda *et al.,* 1990; Jean *et al.,* 1990; Nowrouzian *et al.,* 1991) and goats (De Rossi *et al.,* 2005) after epidural xylazine injection.

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 body temperature have not been well documented in dogs. This study therefore reports on the effects of epidural lidocaine, xylazine and their combination on body temperature at recommended dosages in dogs.

MATERIALS AND METHODS

The study was accepted and carried out according to biosafety, animal use and ethics regulations of the Faculty of Veterinary Medicine, University of Nairobi.

Animals

Fifteen healthy mongrels, comprising males (n=7) and females (n=8) aged 3-5 years were used for the study. Only intact male and intact, non-pregnant female dogs were used for the study. Once acquired, the dogs were screened for diseases by clinical examination and laboratory assessment of the blood. Dogs were then given 7 days to acclimatize to the new environment. Digital abdominal palpation and physical characteristics were used to assess pregnancy status in female dogs. Dogs were housed individually in kennels and provided food once per day. Water was provided ad libitum.

Study design

The fifteen dogs were randomly divided into three treatment groups, such that each group had five dogs. The first treatment involved lumbosacral epidural administration of lidocaine without epinephrine (Lidocaine injection B.P 2%, Macs Pharmaceuticals Ltd, Nairobi, Kenya) at a dosage of 4 mg/kg body weight. The second treatment involved lumbosacral epidural administration of xylazine (Agrar, Agrar Holland BV, Scest Holland) at a dosage of 0.6 mg/kg body weight. The third treatment involved lumbosacral epidural administration of lidocaine-xylazine mixture at half the dosage of each individual drug (lidocaine at 2 mg/kg body weight and xylazine at 0.3 mg/kg body weight). Food and water was withheld from the dogs on the morning of the trials. The body weight of each dog was determined on each occasion prior to the study.

Administration of drugs and monitoring

Dogs were sedated 30 minutes before administration of epidural drugs using acepromazine (Aceprom Inj, Centaur Labs, Isando) at a dosage of 0.1 mg/kg body weight injected intramuscular 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. An empty 5 ml syringe was attached to the needle and suction was then applied to confirm correct needle placement by inability to aspirate blood or cerebrospinal fluid (CSF). About 1 ml of air was then injected to ascertain

loss of resistance to injection as a further proof of correct needle placement. In all treatments, the drugs were injected 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. This was achieved by adding sterile saline solution to make the difference in calculated volume of drug injected in all the five dogs per group equal. The treated dog was supported in sternal recumbency for 3 minutes following drug injection to achieve a bilateral rather than unilateral blockade.

Rectal temperature was assessed at regular intervals: at baseline (5 minutes before epidural injection, defined as minute 0) and 5, 10, 15, 30, 45, 60, 75, 90, 120, 150, 180, 210 and 240 minutes after injection. The rectal temperature was measured using a digital clinical thermometer (Omnisurge, Johannesburg- South Africa).

Data analysis

Data was expressed as means ± standard deviation (SD) of the 5 dogs. The measured temperature variables were compared within and between treatments groups using ANOVA for repeated measures. Where a significant difference was indicated by ANOVA, Bonferonni corrected student t-test was employed as post-hoc test. P value of <0.05 was accepted as being significant in all comparisons.

RESULTS

Significant changes occurred in mean rectal temperature of dogs in all the three groups following epidural administration of the three drug regimes. Dogs injected with lidocaine had significantly ($P< 0.05$) lower mean rectal temperature from 15 minutes post-drug injection through to the end of monitoring period as compared to baseline value (Table 1). Dogs injected with xylazine had significantly ($P< 0.05$) lower mean rectal temperature, starting at 30 minutes post drug injection through to 180 minutes as compared to baseline value (Table 1). On the other hand, dogs injected with the drug combination lidocaine-xylazine had significantly ($P< 0.05$) lower mean rectal temperature starting at 15 minutes post-drug injection, through to 150 minutes as compared to baseline value (Table 1).

Table 1. Means ± SD of rectal temperature (^{o}C) following epidural administration of lidocaine, xylazine and lidocaine-xylazine in dogs

Time (Minutes)	Rectal temperature (°C)		
	Lidocaine	Xylazine	Lidocaine-xylazine
0	38.6±0.3	38.2±0.4	38.4±0.3
5	38.4±0.2	37.9±0.9	38.1±0.6
10	38.3±0.3	38.0±0.4	38.0±0.5
15	38.1±0.3 *	38.0±0.5	37.8±0.4 *
30	37.9±0.3 *	37.6±0.5 *	37.5±0.5 *
45	37.7±0.3 *	37.2±0.3 *	37.1±0.3 *
60	37.7±0.4 *	36.8±0.5 *	36.7±0.5 *
75	37.6±0.5 *	36.7±0.5 *	36.6±0.5 *
90	37.7±0.4 *	36.6±0.6 *	36.4±0.6 *
120	37.7±0.4 *	37.0±0.6 *	36.6±0.9 *
150	37.6±0.5 *	37.1±0.5 *	36.9±2.0 *
180	37.8±0.4 *	37.6±0.4 *	37.0±1.1
210	37.8±0.4 *	37.9±0.4	37.2±1.0
240	37.9±0.5 *	38.1±0.5	37.5±1.0

Values are expressed as means ± SD (n=5)
*Within column, indicate values differ significantly (P< 0.05) from the baseline values.

The lowest mean rectal temperature (36.4 ± 0.6 °C) recorded after epidural injection was observed in lidocaine-xylazine group at 90 minutes post drug injection, followed by xylazine group (36.6±0.6 ^{o}C) and lastly lidocaine group (37.6±0.5 ^{o}C) at 75 minutes post drug injection (Figure 1). This indicated a drop in mean rectal temperature of 2.0 °C, 1.6 °C and 1.0 °C in lidocaine-xylazine, xylazine and lidocaine group, respectively (Table 1).

At the end of the 4 hours monitoring period, the mean rectal temperature of the dogs in the lidocaine group remained significantly lower as compared to the baseline values (Table 1). Groupwise comparison revealed that dogs injected with lidocaine (37.9± 0.3 °C) had significantly ($p<0.05$) higher mean rectal temperature compared to those injected with xylazine (37.5 ± 0.6 °C: p= 0.02) and lidocaine-xylazine (37.3 ± 0.6 °C: p= 0.003) (Figure 2). There was no statistically significant difference (p= 0.37) in the mean rectal temperature between xylazine and lidocaine-xylazine treatment groups (Figure 2).

Shivering was a common side effect of the drugs following their administration affecting 20% of the dogs in the lidocaine group, 60% of dogs in the xylazine group and 80% of those in the lidocaine - xylazine group.

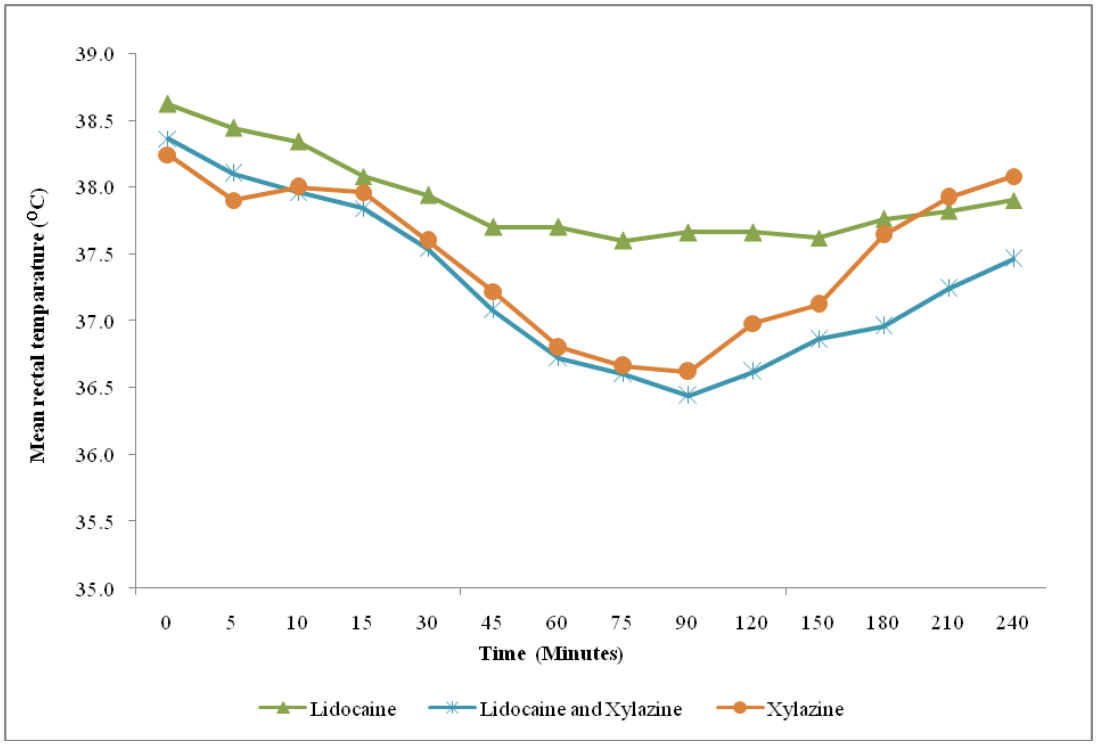

Figure 1. Temporal change in mean rectal temperature (°C) following epidural administration of lidocaine, xylazine and lidocaine-xylazine in dogs

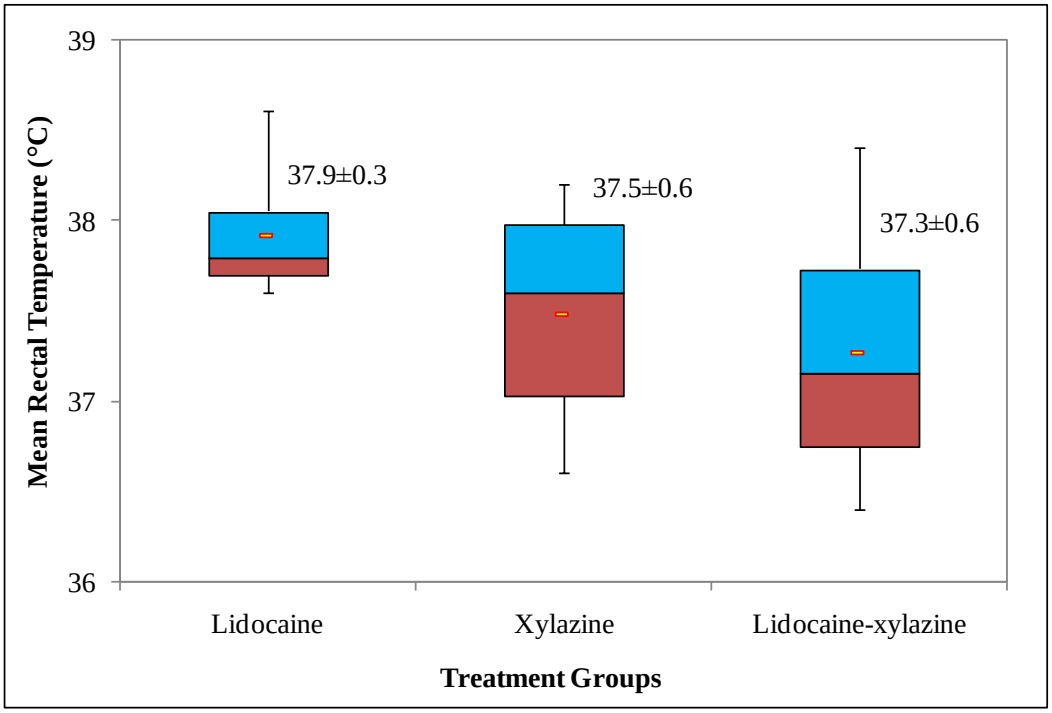

Figure 2. Comparison of mean rectal temperature (°C) following epidural administration of lidocaine, xylazine and lidocaine-xylazine in dogs.

DISCUSSION

In this study, decrease in mean rectal temperature was observed following epidural administration of both individual drugs and the drug combination. This observation may partly be attributed to acepromazine that was injected 30 minutes prior to epidural injections for the purpose of sedation. Acepromazine is a phenothiazine neuroleptic agent which acts by blocking post-synaptic dopamine receptors in the central nervous system (CNS) and depresses portions of the reticular activating system which assist in the control of body temperature, basal metabolic rate, emesis, vasomotor tone, hormonal balance, and alertness (Lemke, 2007; Vesal *et al.,* 2011).

Notably, the level of fall in mean rectal temperature was more profound where xylazine was administered alone or in combination with lidocaine. Decline in mean rectal temperature has been reported in dogs following epidural administration of xylazine (Mohammad, 2003). However, Adentuji *et al.,* (2001) reported non-significant changes in mean rectal temperature of dogs following epidural administration of lidocaine.

The decrease in mean rectal temperature after xylazine administration may be due to generalized sedation, decrease in metabolic rate, muscle relaxation and CNS depression. Alpha-2 adrenoceptor agonists are known to induce prolonged depression of thermoregulation (Ponder and Clarke, 1980). These agents depress the hypothalamic noradrenergic alpha-2 receptors to cause hypothermia (MacDonald *et al.,* 1988). Further, it is possible that alpha-2 agonists act through several mechanisms, apart from CNS depression to cause hypothermia. This is supported by Virtanen, (1986) who reported that hypothermia could not be prevented in dogs by prior administration of yohimbine, an alpha-2 agonist antidote.

Significant decrease in mean rectal temperature as seen in this study was also probably due to fall in the ambient temperature during the course of the trial. Hypothermia as recorded in this study might also be attributed to reduced basal metabolic rate and muscle activity, on top of depression of thermoregulatory centre (Ponder and Clarke, 1980) by acepromazine and xylazine.

When changes in rectal temperature were compared between groups, dogs injected with the drug combination were found to have a significantly lower rectal temperature compared to dogs injected with lidocaine. These observations may be attributed to the synergistic effects of lidocaine and xylazine when administered together. However regardless of the combinations, xylazine could be the most incriminated drug causing hypothermia owing to the fact that there was no significant temperature difference between xylazine and lidocaine-xylazine combination.

Hypothermia in veterinary patients is defined as a decrease in normal body temperature below 37° C (Matsuzaki *et al.,* 2003) and can be categorized as mild hypothermia (body temperature between 32 and 37° C), moderate hypothermia (body temperature between 28 and 32° C) and severe hypothermia (body temperature below 28° C) (Oncken *et al.,* 2001). In this study, dogs in xylazine and lidocaine-xylazine groups suffered mild hypothermia between 60 and 120 minutes and 60-180 minutes post drug administration, respectively.

Hypothermia has serious physiological implication in veterinary patients. This effects include prolonged anaesthesia

recovery time, acute renal tubular necrosis, increased hemorrhage, increased arterial blood pressure, delayed oxygen-hemoglobin dissociation, mental derangements ranging from depression to coma and diminished resistance to infection (Armstrong *et al.,* 2005).

Shivering was observed in 4 dogs in lidocaine-xylazine group, 3 dogs in xylazine group and one dog in lidocaine group. Shivering is a form of thermogenesis employed by the body in response to fall in body temperature (Waterman, 1975). The high number of dogs shivering in lidocaine-xylazine group correlates well to the greatest decline in body temperature (2.0 ° C) in this group compared to the others. Shivering is costly in terms of energy, to a patient recovering from anaesthesia.

In conclusion, all drugs administered caused decrease in body temperature with dogs injected with xylazine and lidocaine-xylazine suffering mild hypothermia lasting for one hour and 2 hours, respectively. This was followed by shivering in the recovery period. It is recommended that when xylazine or lidocaine-xylazine drug combination is used for epidural anaesthesia in dogs, monitoring of body temperature be enhanced so as to mitigate development of hypothermia in a timely manner. Patients under these drugs regimes can benefit from better temperature management perioperatively. Some of the perioperative measures that can be taken to minimize hypothermia include insulation using blankets and beddings to avoid contact with cold surgical tables; minimizing use of excessive scrub solutions or spirit when preparing for surgery; administering warm intravenous fluids and keeping operating rooms warm.

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