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RESEARCH ARTICLE

Effects of epidural Ketamine, Xylazine and their combination on body temperature in acepromazine-sedated dogs

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Abstract

A study was carried out to compare the effects of lumbosacral epidural ketamine, xylazine and their combination on body temperature in dogs. Fifteen healthy dogs were randomly assigned to three groups of five animals each. The first group was injected with 5% ketamine at 2.0 mg/kg body weight, the second with 2% xylazine at 0.6 mg/kg body weight and the third with the drug combination of ketamine and xylazine at 1.0 and 0.3 mg/kg respectively, in the same syringe. Changes in rectal temperature of the dogs were recorded over a 4-hour monitoring period.

Significant ($P < 0.05$) decline in rectal temperature was observed in all the three groups. The ketamine-xylazine drug combination was associated with a decrease in mean rectal temperature of up to 1.9° C; xylazine, 1.62 ° C and ketamine, 1.1 ° C. At the end of the 4- hour monitoring period, rectal temperature of dogs in the ketamine group remained significantly lower as compared to baseline values. Dogs injected with ketamine-xylazine had significantly ($P < 0.05$) lower mean rectal temperature when compared to dogs injected with the individual drugs. Shivering was a common side effect in 60% of dogs in the xylazine group and 80% of those in the ketamine-xylazine group.

It was concluded that epidural ketamine, xylazine and their combination caused significant decline in body temperature even in the absence of any surgical manipulation. In clinical setting, this has both morbidity and mortality implications, especially in small animal surgical patients, in the post-operative period.

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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). Epidural anaesthesia in dogs has been used as an adjunct to general anaesthesia with the aim of providing superior peri-operative analgesia (Hendrix et al., 1996) and reducing the dose requirements for general anaesthetic agents, especially inhalant anaesthetics that cause a dose-dependent cardiopulmonary depression (Tendillo et al., 1995; Torske and Dyson, 2000). This advantage (reduction in dose) can be of value particularly in general anaesthesia of high risk patients (Jones, 2001).

Xylazine, an alpha-2 adrenoceptor agonist when administered epidurally 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 (Adentunji 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.

On the other hand, ketamine is a dissociative anaesthetic that produces analgesia by acting on N-methyl-D-aspartate (NMDA) receptors located centrally and peripherally (Jones et al., 2001; Liu et al., 2001). Epidural ketamine has been used to produce analgesia in dogs (Martin et al., 1997; Amarपाल et al., 1999; Hamilton et al., 2005). However, there are no reports on the effects of epidural ketamine on body temperature in dogs.

In recent years, the ketamine-xylazine combination has been used in dogs because of the resultant superior analgesia and stable cardiopulmonary parameters. However, the effects of epidural ketamine and ketamine-xylazine combination on body temperature in dogs have not been explored. This study therefore reports on the effects of epidural ketamine, xylazine and their combination on body temperature at recommended dosages in dogs.

MATERIAL 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 5% Ketamine hydrochloride (Ketamine Hydrochloride injection USP, Rotexmedica, Trittau Germany) at a dosage of 2.0 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 xylazine-ketamine mixture at half the dosage of each individual drug (ketamine at 1.0 mg/kg and xylazine at 0.3 mg/kg).

Food and water were 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.

Rectal temperature ($^{\circ}\text{C}$) was 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 were expressed as means (\pm SD) of the 5 dogs. The temperature data were analyzed 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

Significant lowering of rectal temperature in dogs occurred steadily and remained below the baseline values throughout the entire monitoring period after epidural administration of the drugs in all the treatment groups as presented in Table 1 and Figure 1. Dogs injected with ketamine had significantly ($P<0.05$) lower rectal temperature ($37.66\pm 0.59^{\circ}\text{C}$) at 30 minutes after drug injection and it remained lower than the baseline value of $38.5\pm 0.67^{\circ}\text{C}$ up to the end of the monitoring period. Dogs injected with xylazine had significantly ($P<0.05$) lower rectal temperature, starting 30 minutes post-drug injection and remaining so through to 180 post-drug injection. Mean rectal temperature for the group at the end of the monitoring period was still lower than baseline value (Table 1 and Figure 1). Dogs injected with xylazine-ketamine drug combination had significantly ($P<0.05$) lower rectal temperature starting at 30 minutes post-drug injection compared to baseline values and this remained so for two hours (Table 1 and Figure 1). The lowest mean rectal temperature recorded after epidural drug injection was with dogs in the ketamine-xylazine group ($36.04\pm 0.52^{\circ}\text{C}$) at 75 minutes, followed by those in xylazine group ($36.62\pm 0.55^{\circ}\text{C}$) at 90 minutes and lastly those in ketamine group (37.40 ± 0.22) at 120 minutes. This represented a drop in mean rectal temperature of 1.9°C for dogs in ketamine-xylazine group, 1.62°C for those in xylazine group and for 1.1°C for those in the ketamine group.

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

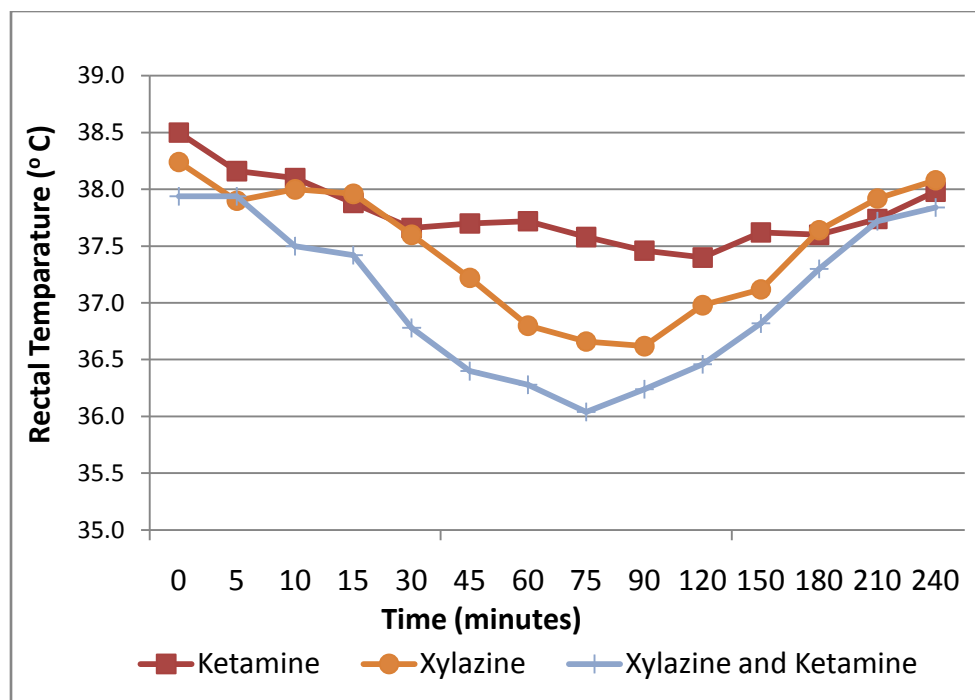


Figure 1: Temporal change in mean rectal temperature (°C) following epidural administration of ketamine, xylazine and their combination in dogs

Table 1: Means (\pm sd; n=5) of temperature (°C) of dogs following epidural injection of ketamine, xylazine and their combination in dogs

Time (Minutes)	Ketamine	Xylazine	Xylazine-ketamine
0	38.50 \pm 0.67	38.24 \pm 0.43	37.94 \pm 0.61
5	38.16 \pm 0.64	37.90 \pm 0.89	37.94 \pm 0.55
10	38.10 \pm 0.54	38.00 \pm 0.43	37.50 \pm 0.90
15	37.88 \pm 0.56	37.98 \pm 0.48	37.42 \pm 1.06
30	37.66 \pm 0.59 *	37.60 \pm 0.50 *	36.78 \pm 0.68 *
45	37.70 \pm 0.52 *	37.22 \pm 0.33 *	36.40 \pm 0.65 *
60	37.72 \pm 0.53 *	36.80 \pm 0.53 *	36.28 \pm 0.61 *
75	37.58 \pm 0.48 *	36.66 \pm 0.50 *	36.04 \pm 0.82 *
90	37.46 \pm 0.42 *	36.62 \pm 0.55 *	36.24 \pm 0.45 *
120	37.40 \pm 0.22 *	36.98 \pm 0.61 *	36.46 \pm 0.58 *
150	37.62 \pm 0.45 *	37.12 \pm 0.46 *	36.82 \pm 0.65 *
180	37.60 \pm 0.42 *	37.64 \pm 0.38 *	37.30 \pm 0.52
210	37.74 \pm 0.31 *	37.92 \pm 0.41	37.72 \pm 0.58
240	37.98 \pm 0.27 *	38.08 \pm 0.48	37.84 \pm 0.59

Values are expressed as means \pm SD (n=5)

*Within column, indicate values differ significantly ($P < 0.05$) from the baseline values.

DISCUSSION

Results from this study provide evidence that hypothermia can occur in dogs following epidural administration of ketamine, xylazine, and ketamine-xylazine combination. The decrease in absolute rectal temperature values observed in the three groups may partly be attributed to acepromazine used to sedate dogs 30 minutes prior to epidural injections. Acepromazine is a phenothiazine neuroleptic agent which acts by blocking post-synaptic

dopamine receptors in the 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).

Although hypothermia was observed in the three groups, the level of decline in temperature was more profound where xylazine was administered alone and in combination with ketamine. Similar observations have been reported previously in dogs following epidural administration of xylazine (Mohammad, 2003). The decrease in rectal temperature by xylazine may be due to generalized sedation, decrease in metabolic rate, muscle relaxation and CNS depression. Alpha-2 adrenoceptor agonists have been reported to induce prolonged depression of thermoregulation (Ponder and Clarke, 1980). These agents have also been found to depress the hypothalamic noradrenergic alpha-2 receptors to cause hypothermia (MacDonald et al, 1988). Furthermore, it is possible that the decrease in rectal temperature by alpha-2 adrenoceptor agonists is not limited to CNS depressant effects, because hypothermia induced by detomidine could not be prevented by prior administration of yohimbine which is an alpha-2 adrenoceptor antagonist (Virtanen, 1986).

There is no report on the effect of epidural ketamine on body temperature in dogs. However, epidural ketamine has been reported not to have any effect on body temperature in buffalo (Singh et al., 2006).

When changes in rectal temperature were compared between groups, dogs injected with ketamine-xylazine were found to have attained significantly lower rectal temperatures compared to dogs injected with individual drugs. It is possible that these observations may be due to the synergistic effects of the combined drugs. Similar findings have been documented previously following epidural administration of xylazine-ketamine combination in buffalo (Singh et al., 2006). However, no significant changes in rectal temperature were noted following epidural administration of xylazine-ketamine combination in goats (Singh et al., 2007).

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 ketamine-xylazine groups suffered mild hypothermia between 60 and 120 minutes and 30-150 minutes post drug administration, respectively.

Hypothermia, especially of the moderate and severe types, has serious physiological implications in veterinary patients. These effects include prolonged recovery time, acute renal tubular necrosis, increased hemorrhage, decreased 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 ketamine-xylazine group, 3 dogs in xylazine group but none in ketamine 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 ketamine-xylazine group correlates well to the higher decline in body temperature (1.9° C) in this group compared to the other groups. Shivering is costly to a patient recovering from anaesthesia due to increased oxygen consumption and energy loss from increased metabolic rate (Waterman, 1975). In conclusion, all drugs administered epidurally caused decrease in body temperature with dogs injected with xylazine and ketamine-xylazine suffering mild hypothermia lasting for one hour and two hours, respectively. Shivering was a notable side-effect observed mostly in dogs under epidural ketamine-xylazine.

It is therefore recommended that when either xylazine or ketamine-xylazine 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 regimens can benefit from better temperature management perioperatively. Some of the perioperative measures that can be taken to minimize hypothermia include insulating the patient against 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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