

# THE INFLUENCE OF EPIDURALLY INJECTED XYLAZINE ON CARDIO-PULMONARY AND RECTAL TEMPERATURES IN GOATS.

D.G. Mpanduji<sup>1</sup>, M.N. Mgasu, S.B.P. Bittegeko and E.K. Batamuzi

*Corresponding Author: <sup>1</sup>Department of Veterinary Surgery and Theriogenology, Faculty of Veterinary Medicine, Sokoine University of Agriculture P.O. Box 3020, Morogoro, Tanzania.*

## SUMMARY

The influences of xylazine on cardiopulmonary and rectal temperature values were investigated in seven Small East African goats. Three doses, 50µg/kg, 100µg/kg and 150µg/kg body weight of xylazine were used. The three doses were administered epidurally to each of the seven goats, with a one-week interval between doses. All doses induced a significantly fall in the mean respiration and heart rates, arterial pressure and rectal temperature values within five minutes ( $P < 0.05$ ). The mean respiration and heart rates depressant effects persisted for the whole 180 minutes observational period. However, the mean arterial pressure depression effect persisted for short period, and was followed by a gradual increase to normal or above normal values. The rectal temperature changes were very mild, and remained within the normal ranges. It is concluded that epidurally administered xylazine at dose ranging from 50µg to 150µg/kg body weight induces a variable cardiopulmonary and rectal temperature changes that are not detrimental to the animal.

## INTRODUCTION

Xylazine is an  $\alpha_2$ -adrenergic receptor agonist with sedative, analgesic and muscle

relaxation properties widely used in horses, cattle, dog and cats, alone or in combination with other anaesthetic agents (Short, 1992). Parenteral (IM or

IV) administration of xylazine results to dose dependent sedation, short duration analgesia and variable cardio-pulmonary depression in many species (Hall and Clarke, 1991, Short, 1992). Dose dependant sedation, recumbency and unconsciousness is reported to be common in ruminants and small animals (Hall and Clarke, 1991). Of the ruminants, goats are reported to be extremely sensitive to xylazine (Deghani et al., 1991). Yeboa and Huvos (1980) reported a severe respiratory depression in goats after parenteral administration of xylazine at 1mg/kg body weight. Recent reports have shown that, epidural administration of xylazine at dose ranging from 50 $\mu$ g to 150 $\mu$ g/kg body weight effectively induces long duration analgesia of the flank and perineal regions in goats (Aithal *et al.*, 1997a,b., Mpanduji *et al.*, 1998). However, no such report has described the effects of different doses of epidurally administered xylazine on the cardio-pulmonary and rectal temperature values in goats. This study reports on the influence of epidurally

injected xylazine on cardio-pulmonary and rectal temperature values at three (50 $\mu$ g, 100 $\mu$ g and 150 $\mu$ g/kg body weight) different doses.

## MATERIALS & METHODS

### Test drug, doses and allocation procedures

Three doses (50 $\mu$ g, 100 $\mu$ g and 150 $\mu$ g/kg body weight) of xylazine (Chanazine<sup>R</sup>, Chanelle pharmaceuticals Ireland) were used in this study.

The test drug was diluted to the final concentrations of 500 $\mu$ g/ml using water for injection. This concentration was achieved by adding 2.5mls of 20mg/ml xylazine to 97.5mls of water. It is from this solution that pre-calculated doses of xylazine were drawn for epidural administration. The purposes of dilutions were to increase the volume of the drug to enhance wide spread into the epidural space.

### Experimental animals

Seven, adult Small East African goats of both sexes were used for this study. The animals were in good health based on clinical and laboratory investigations. The goats were confined in well-ventilated spacious pen at night

and allowed to graze freely for 8 hours daily. Twelve hours prior to experiment, animals were confined and fasted but provided with water. The heart rate, respiration rate, rectal temperature and blood pressure were determined and recorded to establish the baseline data.

### **Experimental design**

The three doses (treatments) were administered to each of the seven goats, with a one-week interval between subsequent treatments.

### **Preparation of the animal for epidural injection**

The lumbosacral region was prepared aseptically to avoid introduction of infectious materials into the lumbosacral epidural space. The area was cleaned, shaved and disinfected using Savlon<sup>R</sup> (cetrimide and chlorohexidine), 70% alcohol and iodine in that order.

A sterile, 18 gauge, 10 cm spinal needle was inserted into the epidural space as described by Gray and McDonell (1986). A pre-calculated dose of  $\alpha_2$ -adrenergic receptor agonist adjusted to total volume of 5mls by addition of water for injection was administered

through the needle previously positioned epidurally. After epidural injection of the test dose, animals were restrained in right lateral recumbency and cardio-pulmonary parameters were monitored and recorded.

### **Clinical parameters**

**Heart and respiration rates; blood pressure and rectal temperature.**

These parameters were measured at time = 0, 5, 10, 15, 20, and 30 minutes, thereafter at 15 minutes intervals up to 180 minutes. The heart and respiration rates were measured by thoracic auscultation using a stethoscope. The systolic and diastolic arterial pressures were measured oscillometrically using the HEM 705 CP digital human prototype (Omron<sup>R</sup>, Omron Corp. Japan) with the cuff placed around the neck. The mean arterial blood pressure (MAP) was calculated as described by Remillard *et al.* (1991). Rectal temperature was recorded continuously using digital thermometer (Exacon<sup>R</sup>, Denmark) with the temperature probe placed deep into rectum.

## Data analysis

Data analysis was performed using a computer package (SAS), general linear model procedure. The main effects (cardio-pulmonary changes and rectal temperatures) were tested for significance as described in the SAS/STAT™ 6.03 release (1988). For each of the tested doses, all the tested parameters at different time intervals were compared to the pre-injection (base line) values. The comparisons between treatments were performed to see if there were any differences between the main effects. When a significant variation was noted, pair wise comparisons were performed at each time point to locate the difference. Data were considered significantly different when  $P < 0.05$ .

## RESULTS

### Effects of the various xylazine doses on respiration rate.

A dose dependant respiratory depression was noted after epidural injection of xylazine. The general trend was a decrease in the mean respiration rate (MRR) throughout the observational

period (Fig 1).

Following epidural administration of xylazine at a dose of  $50\mu\text{g}/\text{kg}$  body weight, the MRR decreased significantly ( $P < 0.05$ ) from pre-injection value of 19.5 to 14.2 breaths/minute. For the  $100\mu\text{g}$  and  $150\mu\text{g}/\text{kg}$  treatments, the MRR decreased from 24 to 14.8 and 22.5 to 15 breaths/minute respectively ( $P < 0.05$ ). These effects occurred at  $t = 25, 10$  and 15 minutes for the 50, 100 and  $150\mu\text{g}/\text{kg}$  treatments respectively.

The MRR depression effect persisted throughout the observational period of 180 minutes for the 50 and  $100\mu\text{g}/\text{kg}$  treatments. The  $150\mu\text{g}/\text{kg}$  treatment was characterized by an initial and significant decrease of the MRR ( $P < 0.05$ ). This effect was followed by a 30 minutes duration at which there were no significant differences ( $P > 0.05$ ) between the pre-injection MRR to the subsequent MRR values. However, 45 minutes later, the MRR significantly decreased again from the pre-injection MRR values ( $P < 0.05$ ). This effect persisted throughout the

observational period. The lowest MRR occurred at  $t=90$ , 135 and 165 minutes for the 50, 100 and 150 $\mu\text{g}/\text{kg}$  xylazine treatments. At this time points, the MRR changed from pre-injection value of 22.5 to 10.5, 24 to 9.5 and 22.5 to 10.5 breaths/minute equivalent to 50.25%, 60.41% and 53.33% decrease in that order. Statistical comparison of the different xylazine treatments showed significant difference ( $P<0.05$ ) on the MRR values. Pair wise comparison of the MRR at each time points showed a significant variation ( $P<0.05$ ) between 100 and 150 $\mu\text{g}/\text{kg}$  treatments at  $t=10$  minutes. At this time point, the MRR value for the 100 $\mu\text{g}/\text{kg}$  treatment was low (14.83 breaths/minute) compared to 21.5 breaths/minute of the 150 $\mu\text{g}/\text{kg}$  treatment. No significant difference was noted between 50 and 100 $\mu\text{g}/\text{kg}$  and between 50 and 150 $\mu\text{g}/\text{kg}$  treatments ( $P>0.05$ ).

### Effects of the various xylazine doses on the cardiovascular functions

#### Heart rate

Epidural injection of xylazine was characterized by initial increase of the mean heart rate

(MHR) followed by a gradual fall (Fig 2). The MHR for the 50 $\mu\text{g}/\text{kg}$  treatment was significantly above (90.5 beats/minute) the normal pre-injection values of 75.0 beats/minute at  $t=5$  minutes ( $P<0.05$ ). Thereafter, the MHR started to decrease. At  $t=15$  minutes, the MHR had decreased significantly to 62.5 beats/minute ( $P<0.05$ ). The 100 and 150 $\mu\text{g}/\text{kg}$  treatments caused a non-significant increase ( $P>0.05$ ) of the MHR within 5 minutes, which was followed by a gradual fall. At  $t=10$  and 15 minutes, the MHR had decreased significantly ( $P<0.05$ ) from the initial pre-injection values of 77.2 to 66.0 and 81.3 to 69.8 beats/minute for the 100 and 150 $\mu\text{g}/\text{kg}$  treatments respectively. In all treatments, the MHR depressant effects persisted until the end of the 180 minutes observation period. The lowest MHR was 55.2, 52.2 and 58.8 beats/minute which occurred at  $t=60$  minutes for the 50 and 150 $\mu\text{g}/\text{kg}$  treatments and at  $t=75$  minutes for the 100 $\mu\text{g}/\text{kg}$  treatment equivalent to 26.4%, 32.4% and 27.6% fall respectively.

Comparison of the different xylazine treatments showed a

highly significant difference on the MHR values. This difference was noted between 100 and 150 $\mu$ g/kg treatments at t=10 and 20 minutes ( $P<0.05$ ) and at t=25 minutes ( $P<0.01$ ) for the same treatment. At all these time points, the MHR values for the 100 $\mu$ g/kg treatment was low compared to that of the 150 $\mu$ g/kg treatment. These values were 66.0 Vs 78.0, 58.8 Vs 72.0 and 55.7 Vs 72.5 beats/minute respectively. No significant difference was noted between 50 and 100 and between 50 and 150 $\mu$ g/kg treatments ( $P>0.05$ ).

### Blood pressure

Initial decrease and subsequent rises of the mean arterial pressures (MAP) characterized all xylazine treatments to normal or above normal values (Fig 3).

The 50 and 100 $\mu$ g/kg treatments showed a significantly low MAP ( $P<0.05$ ) at t=5 and 10 minutes. At these time points, the MAP had already decreased from the pre-injection value of 102.7mmHg to 71.7mmHg and 109.0 to 86.7mmHg respectively.

The depressant effect persisted

for 40 minutes and 20 minutes respectively, after which it started to rise towards the normal or even above normal values.

The MAP for the 150 $\mu$ g/kg treatment showed a non-significant fall for 10 minutes after which it started to rise to normal or above normal values. At t=165 and 180 minutes, the MAP was above the normal pre-injection values ( $P<0.05$ ). The tendency to return to normal pre injection pressure was faster in higher than in low dose treatments.

The lowest MAP values were noted at t=15 minutes for both 50 and 100 $\mu$ g/kg treatments and at t= 10 minutes for the 150 $\mu$ g/kg treatment. These values were 67.3mmHg, 81.7mmHg and 90.3mmHg equivalent to 34%, 25% and 11.5% decrease for the 50, 100 and 150 $\mu$ g/kg treatments respectively.

Comparison of the various xylazine treatments showed a very high significant variation on the MAP values ( $P<0.001$ ). Pair wise comparison of the MAP at different time points showed significant variations between 50 and 100 $\mu$ g/kg

treatments at  $t=45$  and 75 minutes, between 50 and 150 $\mu\text{g}/\text{kg}$  treatments at  $t=5$ , 15, 20, 45-105, 150, 165-180 minutes and between 100 and 150 $\mu\text{g}/\text{kg}$  treatments at  $t=150$  and 180 minutes. At  $t=45$  and 75 minutes, the MAP of the 50 $\mu\text{g}/\text{kg}$  treatment was significantly lower ( $P<0.05$ ) as compared to that of 100 $\mu\text{g}/\text{kg}$  treatment. At  $t=5$ , 15, 20, 60-150 and 180 minutes, the MAP for the 150 $\mu\text{g}/\text{kg}$  treatment was significantly higher ( $P<0.05$ ) compared to that of the 50 $\mu\text{g}/\text{kg}$  treatment. A significant difference ( $P<0.05$ ) was noted at  $t=165$  minutes between 50 and 150 $\mu\text{g}/\text{kg}$  treatments. At this point, the MAP value for the 150 $\mu\text{g}/\text{kg}$  treatment was 124mmHg compared to 91.1mmHg value respectively. For the 100 and 150 $\mu\text{g}/\text{kg}$  treatments, the 150 $\mu\text{g}/\text{kg}$  treatment had significantly higher MAP values ( $P<0.05$ ). From this observation it showed that, higher dosed had higher MAP values.

#### **Effects of various xylazine doses on rectal temperature**

Epidural injection of xylazine was characterized by a non-significant increase ( $P>0.05$ ) of the rectal temperature (RT)

which was followed by a gradual fall (Fig 4). At  $t=60$  minutes, the 50 $\mu\text{g}/\text{kg}$  treatment had already lowered the RT from the pre-injection value of 39.0°C to 38.3°C ( $P<0.05$ ). The 100 and 150 $\mu\text{g}/\text{kg}$  treatments did not cause a notable effect on the RT. In these groups, RT values remained within the normal ranges throughout the observational period ( $P<0.05$ ).

Comparisons of the various xylazine treatments at different time points on RT values showed a very high significant variation ( $P<0.001$ ). Pair wise comparisons of the RT values showed a significant difference ( $P<0.05$ ) on the RT values between 50 Vs 100 $\mu\text{g}/\text{kg}$  treatments and a high significant difference ( $P<0.01$ ) between 100 Vs 150 $\mu\text{g}/\text{kg}$  treatments. These differences were noted at 0-5 minutes and 0-180 minutes respectively. At  $t=0-5$  minutes, the RT value for the 50 $\mu\text{g}/\text{kg}$  treatment were significantly higher ( $P<0.05$ ) compared to the 100 $\mu\text{g}/\text{kg}$  treatment. Similar differences occurred between 150 $\mu\text{g}/\text{kg}$  and 100 $\mu\text{g}/\text{kg}$  treatment. No difference was noted between the 50 Vs 150 $\mu\text{g}/\text{kg}$  treatments ( $P>0.05$ ).

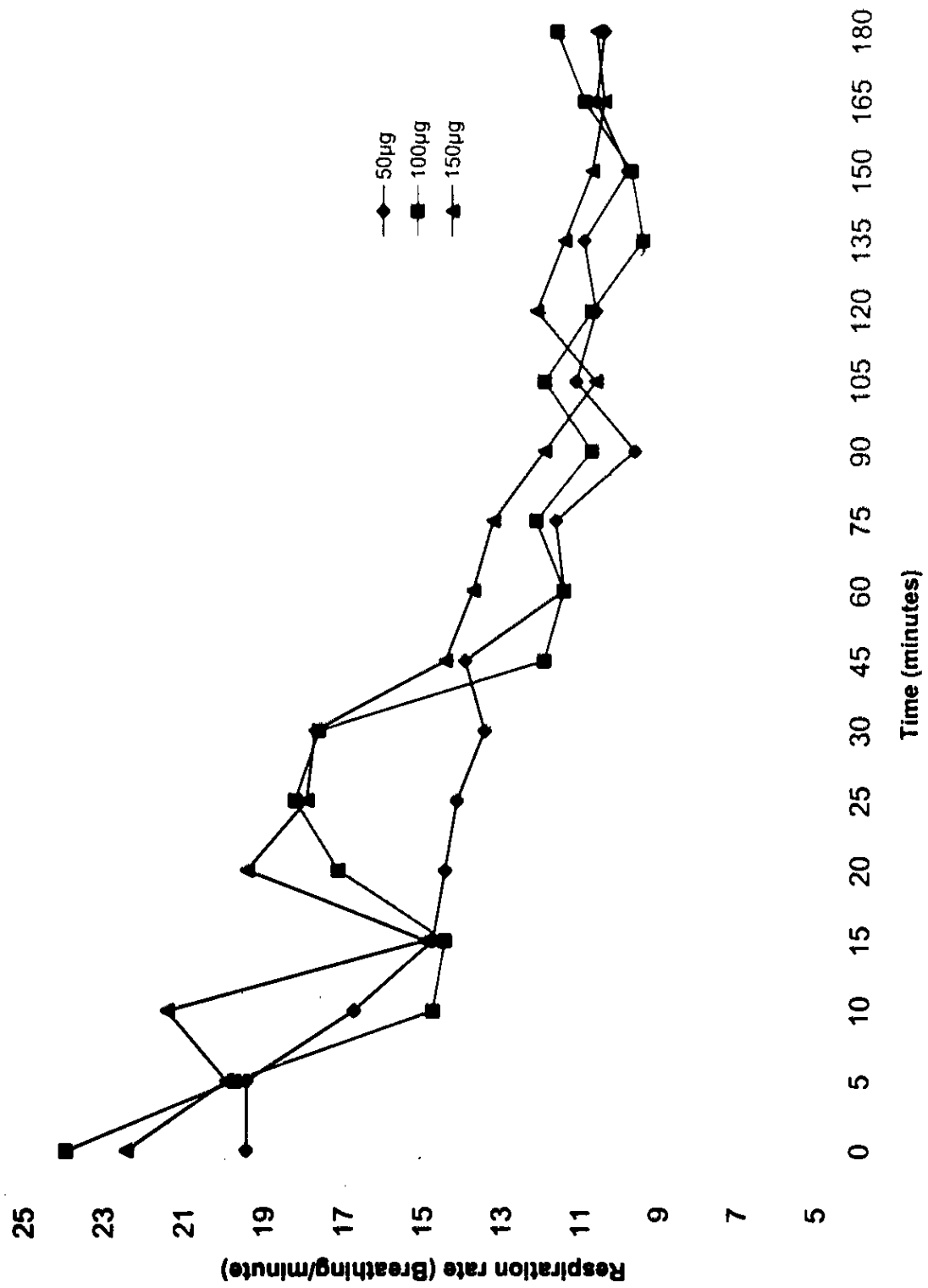
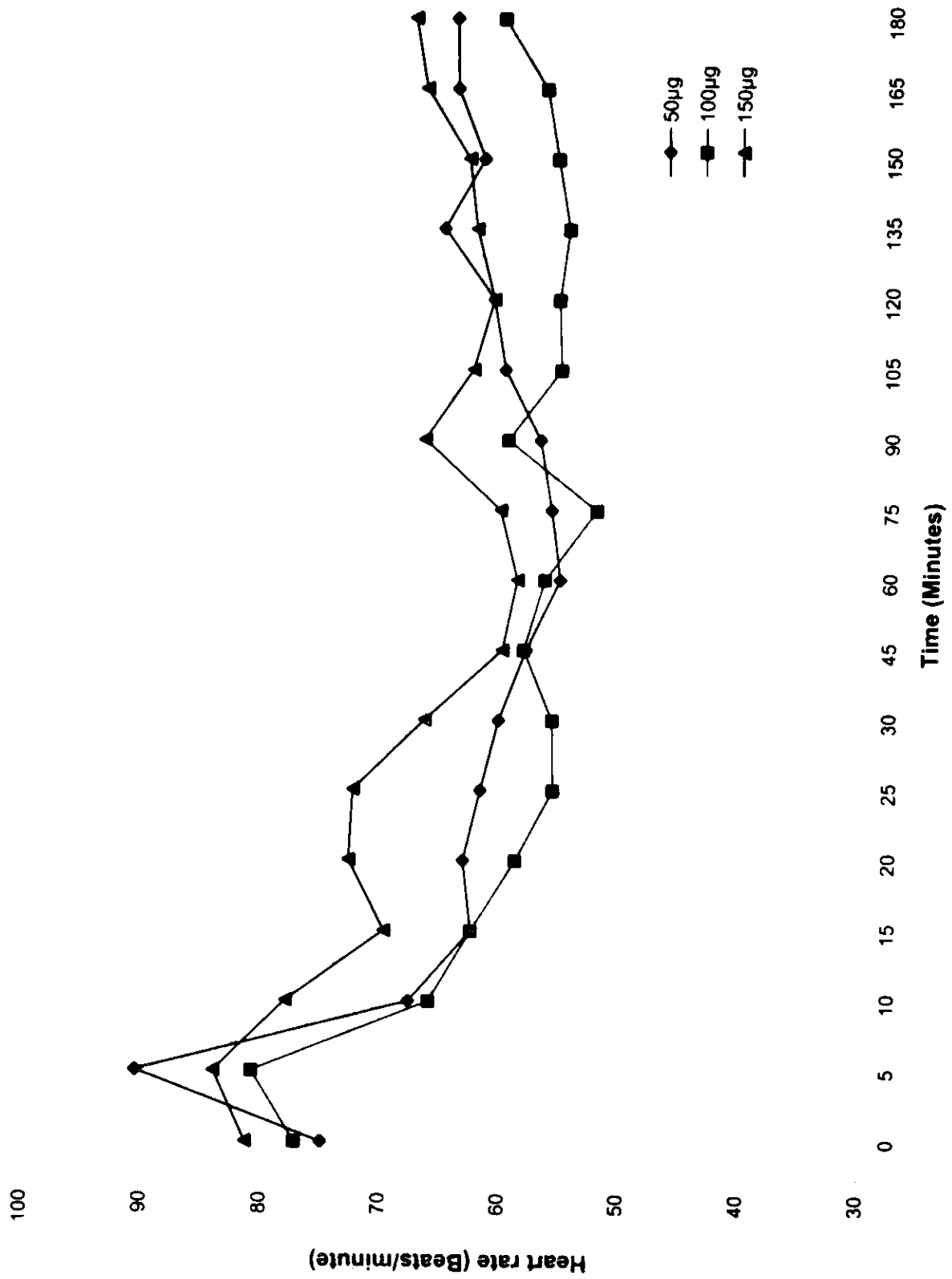


Fig 1: Effects of epidurally injected xylazine on respiration rate in goat.



**Fig 2: Effects of epidurally injected xylazine on heart rate in goat.**

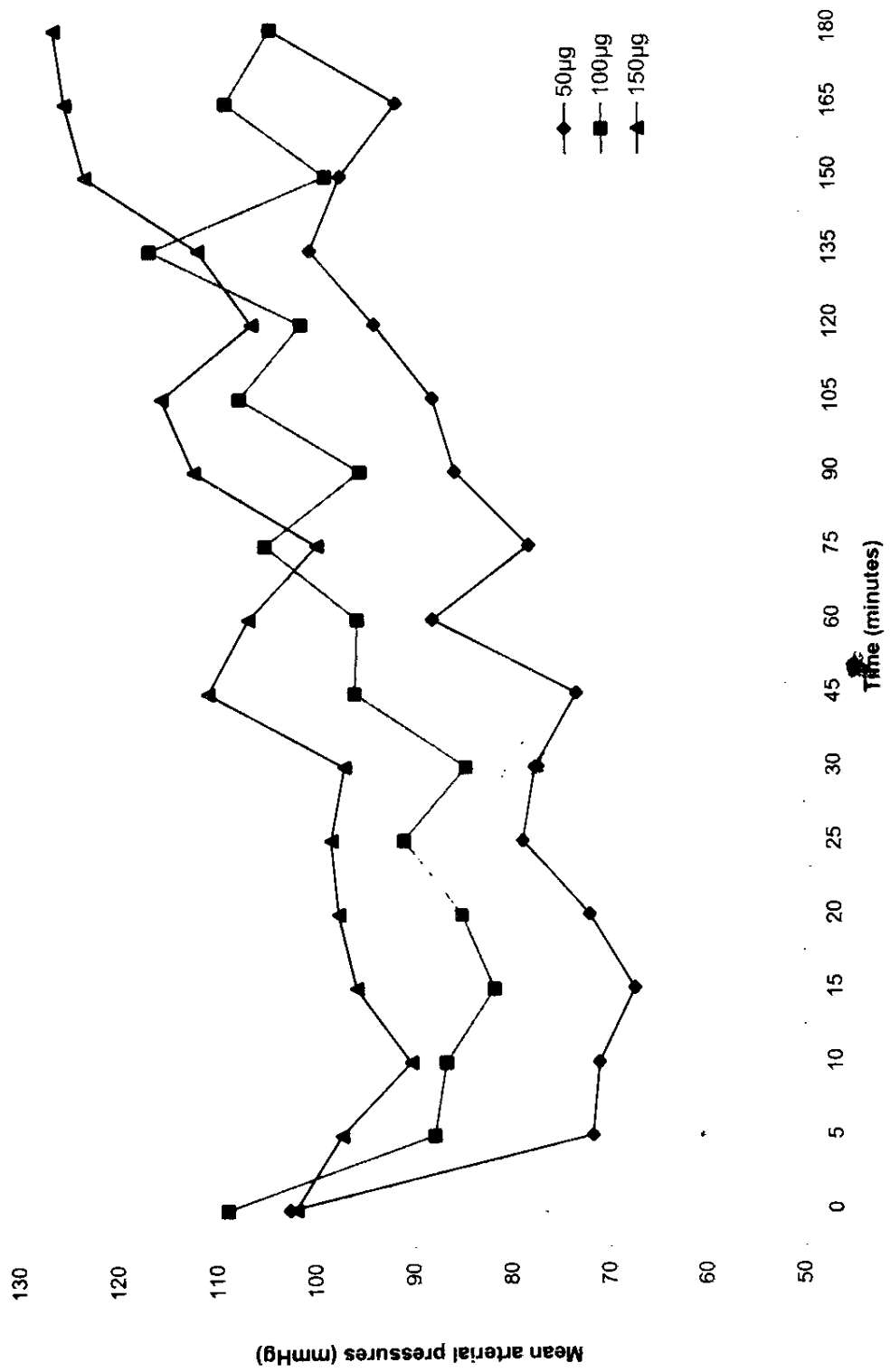


Fig 3: Effects of epidurally injected xylazine on mean arterial pressures (MAP) in goat.

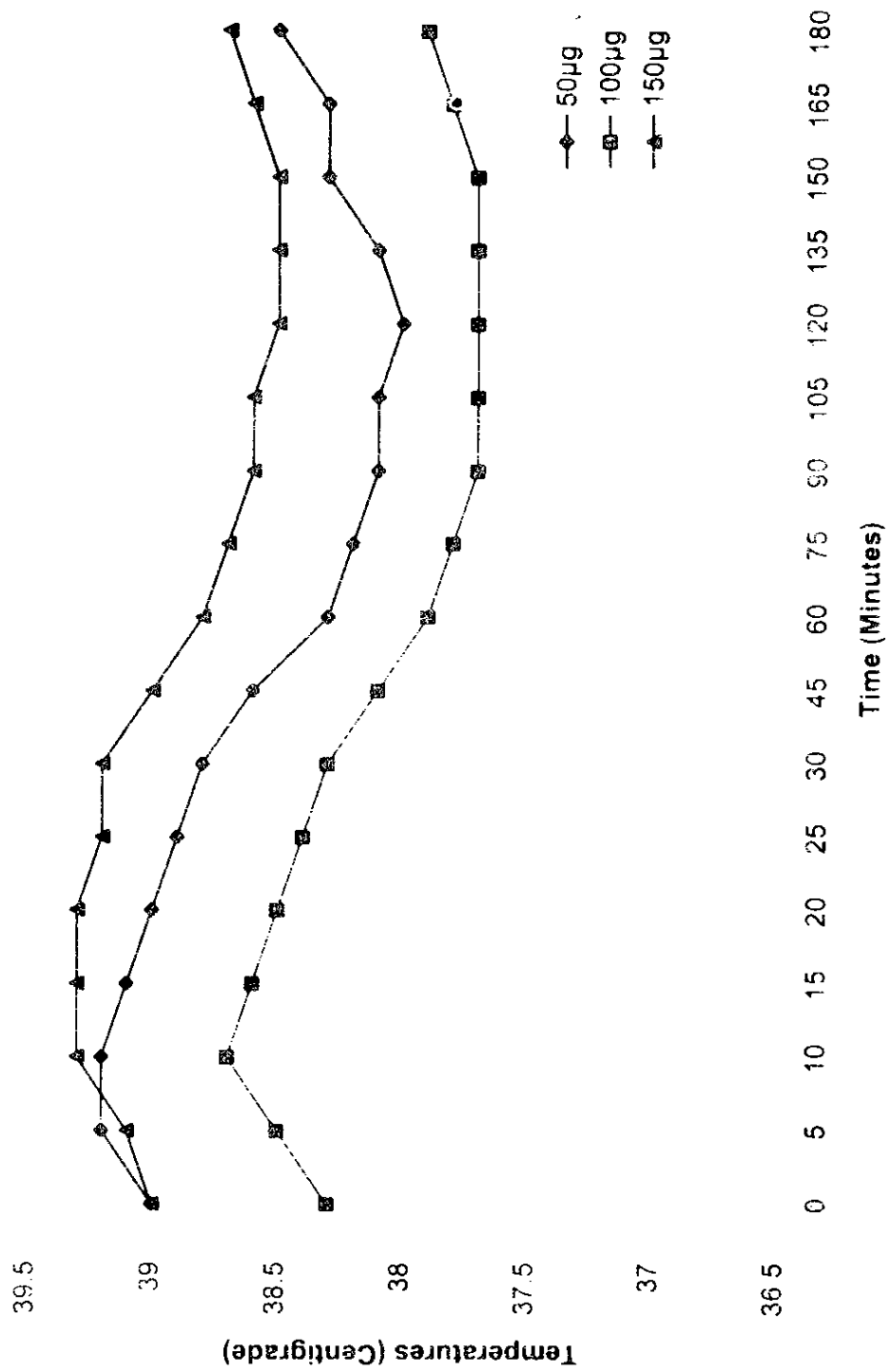


Fig 4: Effects of epidurally injected xylazine on rectal temperatures in goat.

## DISCUSSION

Variable cardio-pulmonary depression and rectal temperature changes were observed in goat after epidural administration of xylazine at dose ranging from 50 $\mu$ g/kg to 150 $\mu$ g/kg body weight.

Respiratory rates (RR) decreased in all treatments within five minutes. In horses, epidural injection of xylazine have been reported to cause mild decrease in RR (Skarda and Muir, 1996a,b). The decrease in RR after epidural injection of  $\alpha_2$ -adrenergic receptor agonists is attributable to the reduced central sympathetic tone and increased vagal tone (Skarda and Muir, 1996b) and due to an increase in airway pressure mediated by peripheral  $\alpha_2$ -adrenergic receptors (Nolan *et al.*, 1986).

All xylazine treatments displayed an initial and non-significant rise in the mean heart rates with a gradual fall. In all treatments, heart rates did not return to the normal pre-injection values throughout the observational period. These observations are in agreement with the

previous reports in horses (England *et al.*, 1992; Wagner *et al.*, 1991) and cattle (Davis, 1980; Greene and Thurmon, 1988) after parenteral (IM or IV) injection and in swine (Ko *et al.*, 1992) and equine (Skarda and Muir, 1996a,b) after epidural injection of xylazine. Bradycardia and second-degree atrioventricular blocks are reported to be common in animals after parenteral injection of xylazine (Davis, 1980; Greene and Thurmon, 1988). A decreased sympathetic outflow from the CNS and vagal reflex from baroreceptor in response to hypertension are believed to be the most likely causes (Davis, 1980; Alitalo *et al.*, 1986).

Epidurally injected xylazine caused initial decrease in the MAP with subsequent rises to normal values. Systemic injection (Short, 1992) and epidural injection (Ko *et al.*, 1992, Skarda and Muir, 1994; 1996a,b) of  $\alpha_2$ -adrenergic receptor agonists in domestic animals is associated with an initial hypertension and subsequent hypotension. The initial hypertension that is normally seen within 5-minutes was not seen in goats.

The study protocol may have failed to detect the changes that occur in connection with or immediately after drug administration since the values were measured at 5 minutes interval. Hypotensive effects are antagonized when the plasma concentration of  $\alpha_2$ -adrenergic receptor agonists goes above 1.5 and 15ng respectively (Wing *et al.*, 1977; Frisk *et al.*, 1984, Frisk and Wibell, 1986) by peripheral vasoconstriction (Langer and Hicks, 1984), through  $\alpha_2B$  adrenergic receptor subtype mediation (Link *et al.*, 1996). The same mechanism may explain the gradual increase in MAP following epidural injection of xylazine seen in this study.

Xylazine showed a mild increase in RT that was followed by subsequent fall to normal temperature. These results are in agreement with previous reports by Skarda and Muir (1994; 1996a,b) where a mild changes in both blood and rectal temperatures were noted after epidural injection of detomidine or xylazine in horses.

## CONCLUSION

The results of the present study indicate that epidural injection of xylazine at dose range of 50 $\mu$ g/kg to 150 $\mu$ g/kg caused a mild cardio-pulmonary and rectal temperature changes that are not detrimental to the animal. Epidural injection of xylazine at dose ranging from 50 $\mu$ g to 150 $\mu$ g/kg body weight can therefore be used in goats for sedation and analgesia.

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