Clinical, cardiopulmonary and haemocytological effects of xylazine in goats after acute exposure to different environmental temperature and humidity conditions

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ABSTRACT

This study was carried out to assess the influence of xylazine administration on clinical, cardiopulmonary and haemocytological variables after acute exposure to different environmental conditions. Xylazine hydrochloride was administered intravenously at 0.1 mg/kg body mass to 6 clinically healthy, castrated male goats. All animals were exposed for 60 min to 3 sets of climatic conditions: 14 °C, 33 % relative humidity; 24 °C, 55 % RH, and 34 °C, 65 % RH. The variables that were measured for a period of 60 min after xylazine administration were sedation, analgesia, salivation, urination, ventilation rate, heart-rate, mean arterial blood pressure, oesophageal temperature, haematocrit, mean corpuscular volume and mean corpuscular haemoglobin concentration. Xylazine induced sedation, analgesia, salivation and urination independently of the 3 environmental conditions. Environment had no influence on the onset, duration and recovery from sedation. In the 14 °C environment, xylazine resulted in a significant decrease in ventilation and heart-rate from baseline values. Significant changes in mean arterial blood pressure, haemoglobin concentration, mean corpuscular volume, haematocrit and red cell count were observed in the 3 environments. Total plasma protein was significantly altered at 24 °C and 34 °C. Acute exposure of goats to different environmental conditions had no significant influence on the clinical, cardiopulmonary and haemocytological variables. Physiological changes induced by xylazine were therefore independent of the environment.

Key words: caprine, cardiopulmonary, haematology, sedation, temperature, xylazine.

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INTRODUCTION

Xylazine, pharmacologically classified as an analgesic as well as a sedative and skeletal muscle relaxant[6], is widely used in biological research and veterinary medicine[18,22]. The drug induces a number of physiological and pharmacological changes in the species in which its use has been studied. The cardiopulmonary and haematological effects of xylazine have been investigated in several animal species including goats[1,5,12,23,24,28,32,35], cattle[3,7,13], sheep[4,9], cats[12], horses[11,17], dogs[21], and donkeys[27].

Xylazine, when injected intravenously in animals, induces hypotension, bradycardia, heart block, ventilatory depression and, in ruminants, marked salivation[6]. In horses[11], dogs[21] and sheep[4], when injected intravenously, xylazine causes partial cardiac conduction blockade with arrhythmia and bradycardia. In ponies, intravenous xylazine produces sino-atrial (SA) block, transient atrioventricular (AV) block and bradycardia within 1 min of injection[17]. A study in heifers revealed that the recovery period, duration of salivation and sedation following xylazine administration were longer in animals acclimatised to hot, humid conditions than in animals under thermoneutral conditions[15]. To our knowledge, the influence of different environmental temperature and humidity conditions on the clinical, cardiopulmonary and haemocytological effects of xylazine in goats has not been described. The purpose of this study was therefore to investigate these effects in goats under different environmental temperature and humidity conditions.

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MATERIALS AND METHODS

Six adult, clinically healthy, indigenous (nondescript African breed), castrated male goats, weighing between 21.0 and 34.0 kg with a mean (± SEM) mass of 28.2 ± 1.0 kg were used. They were housed indoors in individual crates and fed a diet of lucerne, hay and water, which were provided *ad libitum*. At least 1 month before commencement of the study, the carotid artery was relocated under halothane anaesthesia to a subcutaneous position in all the animals . The protocol for this study was approved by the Ethics and Research Committees of the Faculty of Veterinary Science, University of Pretoria.

A single group, 3-phase repeated-measures design was used to study the effect of environmental temperature and humidity on some clinical, cardiopulmonary and haemocytological effects of xylazine in 6 goats. These effects were monitored repeatedly for a period of 60 min in the goats during low, medium and high temperature and humidity exposure treatment phases. A washout period of at least 7 days was allowed between treatment phases. The experiments in this study were conducted in temperature- and humidity-controlled environments. Phase 1 of the study was conducted in the medium temperature and humidity environment with room temperature set at 24 ± 1 °C and a relative humidity of 55 ± 1 %. Phase 2 of the study was conducted in the high temperature and humidity environment with room temperature set at 34 ± 1 °C and a relative humidity of 65 ± 1 %. Phase 3 of the study was conducted in the low temperature and humidity environment with the room temperature set at 14 ± 1 °C and a relative humidity of 33 ± 1 %. The temperature and humidity were set 12 h before any experiment began to ensure uniformity of conditions in the rooms. Between experiments, the goats were housed and fed in individual crates in housing premises without temperature and humidity control. Before any experiment was carried out, the goats were starved for 24 h and water was withheld

for 12 h. On the day of the experiment, each goat was weighed and taken into a preparation room adjacent to the temperature- and humidity-controlled room.

In the preparation room, the goats were restrained in lateral recumbency on a waterproof foam mattress. The jugular furrows on both sides of the neck were surgically prepared. An 18 G intravenous catheter (Jelco®, Critikon) was percutaneously introduced into the left jugular vein, flushed with heparinised saline, capped and sutured to the skin with nylon No. 2/0 (Ethilon) sutures. Another 20 G catheter (Medican®, Medical Specialities) was percutaneously introduced into the subcutaneously situated right carotid artery, flushed with heparinised saline, capped and sutured to the skin with nylon sutures. The animals were then transferred to the temperature- and humidity-controlled rooms. Lateral recumbency was maintained. A multiparameter physiological monitor was used to monitor the mean arterial blood pressure and heart-rate (Propaq® 104EL, Protocol Systems, Oregon, USA). A calibrated strain-gauge blood pressure transducer was connected to the carotid artery *via* non-compliant tubing and a 3-way stopcock. The zero-point for the strain-gauge blood pressure transducer was taken at the level of the sternum. After a stabilisation period of 10–15 min, baseline readings were recorded. Xylazine hydrochloride (Rompun®, Bayer Animal Health, Isando, South Africa) was injected intravenously at a dose of 0.1 mg/kg body mass over a period of 60 sec. The temperature probe was introduced *via* the ventral nasal meatus to the proximal oesophagus. The ventilation rate was determined using a capnograph (Normocap 200, Datex Instrumentarium Corporation, Helsinki), or by counting the thoracic excursions over a 1-min period. The ventilation rate, heart-rate, and mean arterial blood pressures were recorded at 'time zero' (baseline) and at 5, 15, 30, 45, and 60 min post-xylazine injection. Venous blood for the determination of haemoglobin concentration, red cell count, white cell count, haematocrit, mean corpuscular haemoglobin concentration, mean corpuscular volume and total protein were drawn from the jugular vein into EDTA tubes at 'time zero' and 15, 30, and 60 min post-xylazine injection. These determinations were made within 6 h of sample collection. All cell counts and blood cell parameters were determined using a System 9000 Diff Model Automated Cell Counter (Serono Diagnostics, Pennsylvania, USA). Total plasma protein was determined using an RA-1000 Analyzer (Technicon Instruments Corporation, New York, USA) based on the Biuret reaction of Weichselbaum and as described by Skeggs and Hochstrasser[39]. Other variables evaluated over the entire monitoring period were sedation, analgesia, salivation, muscle relaxation and recovery time. Sedation was assessed by observing for drooping of the upper eyelids and protrusion of the tongue. Analgesia was assessed by the response of the goats to needle pricks on the flank, thorax, coronary band and manual pinching of the interdigital skin. Muscle relaxation was evaluated according to the muscle tone of the mandible and uppermost fore and hind limbs during passive flexing and extending. Recovery time was considered to be the time when the animals were able to stand unassisted.

Data analysis

The data were analysed on a personal computer equipped with statistical software (Sigma Stat 2.0, Jandel Scientific Software®, Jandel Corporation, San Rafael, California, USA). Results are presented as mean and standard error of the mean. To test for significance of the effect of treatment over time as well as for differences among treatments between groups, data collected over time were analysed using a 2-way repeated-measures ANOVA. When a significant effect of treatment was observed, comparisons between treatments were performed using 1-way ANOVA for repeated measures followed by Bonferroni's *t*-test to examine for least significant difference. Significant changes with time within any group were also analysed using 1-way ANOVA for repeated measures followed by Bonferroni's *t*-test to examine deviation from control (baseline, 'time zero') values. Where the data were either not normally distributed or the equal variance test failed, they were analysed using Friedman repeated-measures ANOVA on ranks followed by Dunnett's method to examine deviations from baseline or 'time zero' (control) values. $P < 0.05$ was considered significant.

RESULTS

Clinical and behavioural effects

Oesophageal temperature decreased from 39.2 ± 0.2 °C to 38.6 ± 0.2 °C at 24 °C environment, increased from 39.3 ± 0.1 °C to 39.8 ± 0.1 °C at the 34 °C environment, and decreased from 39.5 ± 0.1 °C to 38.0 ± 0.2 °C at the 14 °C environment. The latter decrease was significantly different from baseline.

Under all environmental conditions, xylazine administration to the goats caused initial excitement and restlessness characterised by bleating, groaning, grunting and limb movements that lasted from 1 to 5 min. Nystagmus was also evident during this period. This was followed by a period of calm and the animals remained sedated for the next 25 to 30 min, with occasional bleating and tail switching observed in some of the goats. Signs of recovery evidenced by leg movements and raising of the head occurred within 40 to 50 min following xylazine administration. At the end of the monitoring period, the jugular vein and arterial indwelling catheters and the oesophageal thermometer probe were removed and the animals were left undisturbed to rise on their own. The mean times required to rise unaided were 73.8 ± 4.9, 70.5 ± 0.8, and 68.0 ± 1.0 min from the time of xylazine administration in the 24, 34, and 14 °C environments respectively. There was no significant difference in the time they took to stand under the different sets of environmental conditions. On standing, all the animals had a stable gait, ate and drank water immediately without any difficulty.

Following intravenous administration of xylazine, salivation started at 6.3 ± 0.8, 5.7 ± 1.4, and 6.5 ± 1.2 min in the 24, 34, and 14 °C environments respectively. Although the amount of saliva was small at the beginning, it became copious in the following minutes and then subsided to very small amounts. The duration of salivation was 45.7 ± 2.0, 45.2 ± 4.6, and 44.3 ± 3.1 min in the 24, 34, and 14 °C environments respectively. There were no significant differences in the time salivation started or the duration of salivation under the different environmental conditions.

Following administration of xylazine to the goats, insensitivity of the abdominal and thoracic skin to pin-pricks was present starting at 7.4 ± 1.5 min in the 24 °C environment and the duration of analgesia was 40.0 ± 3.7 min. In the 34 °C environment, analgesia of the thorax and abdomen was present at 6.17 ± 0.8 min that lasted for 43.8 ± 3.9 min. The onset of analgesia was at 5.5 ± 0.5, and the duration was 39.5 ± 2.2 min in the 14 °C environment. In all cases, there was no analgesia distal to the coronary band. The analgesia of the abdominal skin persisted longer than that of the thoracic wall skin. The onset and duration of analgesia were not statistically different under the different environmental conditions.

Xylazine induced voiding of large amounts of urine under all environmental conditions after 21.0 ± 1.9 min and also after 69.6 ± 3.4 min. Xylazine provided good muscle relaxation in all the goats under all conditions and this lasted during the 25 to 30 min of sedation.

Cardiopulmonary and haemocytological effects

The trend in heart-rate following intravenous injection of xylazine in the goats under all environmental conditions was similar (Fig. 1). Within the 1st minute following injection of the drug, half of the goats exhibited bradycardia and atrioventricular (AV) block, followed by tachycardia. Bradycardia alternated with tachycardia in most of the goats during the first 5 min after administration of xylazine, and this persisted for up to 10 min in some goats. Mean heart-rates declined in all 3 environments for the rest of the monitoring period. The heart-rates had not returned to baseline values at the end of the monitoring period. The mean heart-rate for the goats exposed to 24 °C decreased from 74.0 ± 6.1 beats/min at 'time zero' to 63.0 ± 6.0 beats/min at 30 min and declined further to 58.0 ± 4.2 beats/min at 60 min post-xylazine injection, a decrease of 22 %. In the 34 °C environment, mean heart-rate increased from baseline value of 76.5 ± 3.9 beats/min to 82.5 ± 11.9 at 5 min and then declined to 66.7 ± 4.4 beats/min at 30 min and then further to 64.3 ± 7.2 beats/min at 60 min, a decline of 16 %. None of these changes were significant compared to baseline values. The mean heart-rates of goats in the 14 °C environment declined from 85.0 ± 10.9 beats/min at time zero to 72.8 ± 9.4 at 30 min and then further to 60.0 ± 3.2 beats/min at 60 min, a decline of 29 %. Mean heart-rate 60 min post-xylazine injection in this group was significantly ($P < 0.05$) lower than the baseline value. There was marked individual variation in heart-rate under the different environmental conditions. Environmental conditions did not in general have a significant effect on heart-rate.

Mean arterial blood pressure (MAP) changes following injection of xylazine were similar under the 3 sets of environmental conditions (Fig. 2). Within 2 min of the injection of the drug, all goats developed arterial hypertension. In the 24 °C environment, MAP rose from 16.1 ± 0.5 kPa at 'time zero' to 20.9 ± 1.0. In the 34 and 14 °C environments, MAP rose from 15.8 ± 0.5 and 14.9 ± 0.5 at 'time zero' to 18.7 ± 0.2 and 18.9 ± 0.7 kPa respectively. Thereafter the MAP started to decrease to a minimum pressure at 15 min of 4.5 kPa in the 24 °C environment. In the 34 and 14 °C environments, maximum decrease in MAP of 5.3 and 4.3 kPa were recorded at 5 min post-xylazine injection, respectively. Following the maximal decline, MAP started increasing in all 3 environments but had not returned to baseline values by the end of the 60-min monitoring period. The MAP values at 5, 15, 30, 45, and 60 min post-xylazine injection were significantly ($P < 0.05$) lower than baseline values under all 3 sets of environmental conditions. There were no significant differences in mean arterial blood pressure attributable to the differences in temperature and humidity in the 3 environments.

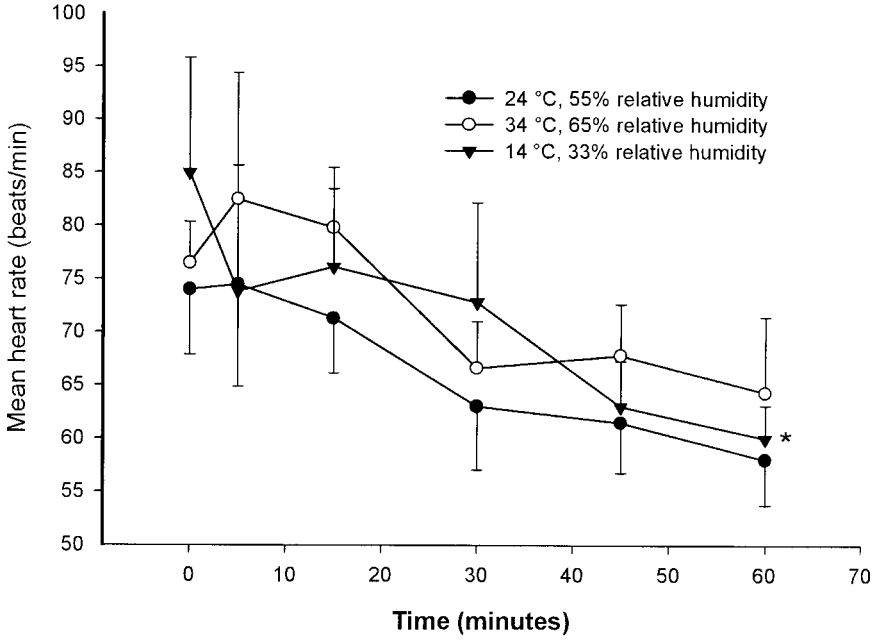

Fig. 1: **Temporal changes** (mean ± SEM) **in heart-rate of goats following intravenous injection of 0.1 mg/kg xylazine under different environmental conditions.** *Significantly ($P < 0.05$) different from values at time zero.

Xylazine resulted in clinically significant changes in ventilation rate under all environmental conditions. Within 5 min of drug administration, the goats exhibited apnoea that lasted up to 1 min in some goats. The apnoea alternated with irregular, laboured breathing, while some goats showed open-mouth breathing and gasping for air. There was also cyanosis of the oral mucous membranes. For the rest of the monitoring period, the breathing pattern alternated between rapid, shallow breathing to deep and slow breathing as evidenced by the thoraco-abdominal movements. Regular breathing patterns were observed in most goats after 45 to 50 min. Ventilation rate varied under the different environmental conditions. In the 24 °C environment, the mean rate increased from the baseline of 28.7 ± 3.2 breaths/min to 31.5 ± 7.0 at 15 min and then decreased to 20.3 ± 2.7 breaths/min

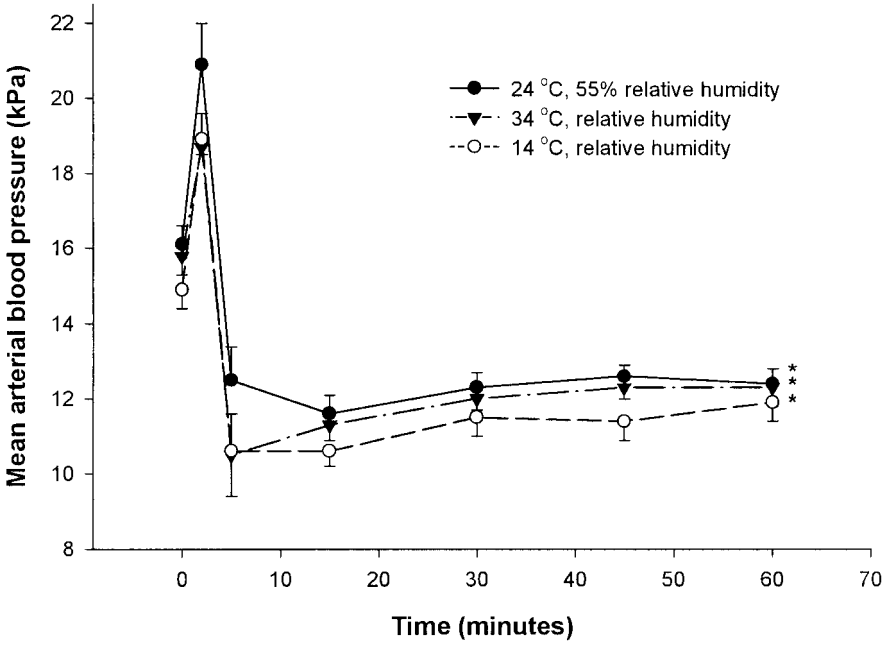

Fig. 2: **Temporal changes** (mean ± SEM) **in mean arterial blood pressure of goats following intravenous injection of 0.1 mg/kg xylazine under different environmental conditions.** *Significantly ($P < 0.05$) different from values at time zero.

Table 1: **Changes in haemocytological variables** (mean ± SEM) **in goats following intravenous injection of 0.1 mg/kg xylazine under different environmental conditions.**

Variable	Temperature (°C)	Time post-xylazine injection (min)			
		0	15	30	60
Hb (g/ℓ)[a]	14	106.3 (± 2.9)	94.8 (± 3.1)*	91.3 (± 3.1)*	93.9 (± 3.5)*
	24	104.0 (± 2.6)	90.3 (± 7.8)*	87.9 (± 2.9)*	89.4 (± 3.1)*
	34	104.2 (± 4.8)	88.2 (± 1.5)*	85.1 (± 2.3)*	88.7 (± 3.4)*
RCC ($\times 10^{12}$/ℓ)[b]	14	17.4 (± 0.6)	15.6 (± 0.3)*	14.9 (± 0.5)*	15.5 (± 0.6)*
	24	17.3 (± 0.5)	15.3 (± 0.4)*	14.6 (± 0.4)*	14.9 (± 0.4)*
	34	17.0 (± 0.5)	14.8 (± 0.3)*	14.1 (± 0.3)*	14.5 (± 0.5)*
TPP (g/dℓ)[c]	14	61.2 (± 1.8)	59.4 (± 1.7)	59.2 (± 1.7)	59.4 (± 1.2)
	24	65.6 (± 1.1)	62.2 (± 0.8)*	61.3 (± 0.9)*	61.4 (± 1.1)*
	34	62.3 (± 1.2)	60.2 (± 1.0)*	59.4 (± 0.7)*	59.1 (± 0.7)*
HT (ℓ/ℓ)[d]	14	0.32 (± 0.01)	0.28 (± 0.01)*	0.26 (± 0.01)*	0.27 (± 0.01)*
	24	0.31 (± 0.01)	0.26 (± 0.01)*	0.26 (± 0.01)*	0.26 (± 0.01)*
	34	0.31 (± 0.01)	0.26 (± 0.01)*	0.25 (± 0.01)*	0.26 (± 0.01)*
MCV (f/ℓ)[e]	14	17.2 (± 0.2)	16.9 (± 0.2)*	16.9 (± 0.2)*	17.0 (± 0.2)*
	24	16.9 (± 0.2)	16.7 (± 0.2)*	16.5 (± 0.2)*	16.5 (± 0.2)*
	34	17.1 (± 0.2)	16.8 (± 0.2)*	16.7 (± 0.2)*	16.7 (± 0.2)*
MCHC (g/dℓ cells)[f]	14	33.3 (± 0.6)	33.8 (± 0.3)	34.3 (± 0.5)	34.8 (± 0.6)*
	24	32.8 (± 0.6)	33.3 (± 1.0)	34.8 (± 0.7)*	35.2 (± 0.8)*
	34	33.5 (± 1.0)	34.0 (± 0.6)	34.0 (± 0.5)	34.8 (± 0.8)
WCC ($\times 10^{9}$/ℓ)[g]	14	18.3 (± 1.3)	15.7 (± 1.1)	14.0 (± 1.1)*	14.1 (± 1.6)*
	24	18.8 (± 2.4)	16.7 (± 2.2)	15.4 (± 1.9)*	16.7 (± 1.6)
	34	16.9 (± 0.9)	13.9 (± 1.1)*	13.0 (± 0.9)*	13.2 (± 1.3)*

*Significantly ($P < 0.05$) different from values at time zero (baseline values).
[a]Haemoglobin concentration; [b]red blood cell count; [c]total plasma protein; [d]haematocrit; [e]mean corpuscular volume; [f]mean corpuscular haemoglobin concentration; [g]white cell count.

at 45 min and from then on it started to increase again. However, these changes were not significant. In the 34 °C environment, the mean rate increased from the baseline of 28.2 ± 1.5 breaths/min to 40.0 ± 7.9 at 5 min, then decreased to 16.7 ± 1.9 breaths/min at 45 min, and then started to rise. Ventilation rate was significantly ($P < 0.05$) lower at 45 min compared to the rate at 5 min in this group. In the 14 °C environment, mean rate declined from baseline at 31.7 ± 1.9 to reach a minimum of 15.7 ± 2.4 at 30. The mean ventilation rates in this environment at 30, 45, and 60 min were significantly ($P < 0.05$) lower than the baseline value. In all of the environments the ventilation rates remained lower than the baseline values at the end of the 60-min monitoring period. Environmental conditions did not have significant effects on the ventilation rate.

The results of the effects of xylazine on the haemocytological variables under the different environmental conditions are shown in Table 1. Xylazine significantly ($P < 0.05$) reduced haemoglobin concentration and mean corpuscular volume 15 min post-xylazine injection until the end of the 60 min monitoring period in all 3 environments. A similar, significant ($P < 0.05$) reduction in total protein over the same period occurred in goats in the 24 and 34 °C environments, while there was no significant change in total plasma protein in the 14 °C environment. Significant ($P < 0.05$) reductions in haematocrit and red cell count occurred at 15, 30, and 60 min post-xylazine injection in all environments. Mean corpuscular haemoglobin concentration increased significantly ($P < 0.05$) 30 and 60 min post-xylazine injection at 24 °C, and 60 min at 14 °C, whereas there was no significant change at 34 °C. Xylazine caused a significant ($P < 0.05$) reduction in the total white cell count at 30 min in the 24 °C environment, whereas this reduction was significant at 15, 30, and 60 min, and at 30 and 60 min in the 34 and 14 °C environments respectively. These variables had not returned to the baseline values by the end of the 60-min monitoring period. Xylazine caused haemolysis, and this was seen in the plasma of all blood samples drawn within the first 5 min following its injection. Environmental conditions did not have significant effects on the variables.

DISCUSSION

Goats are more sensitive to xylazine than sheep, and doses of 0.05 mg/kg may result in profound sedation for 12 or more hours[12]. The time of onset of sedation, the duration of action, and recovery from xylazine in goats varies, and may be influenced by dose and route of administration[12,19,28,32,35]. In this study, xylazine administration to the goats initially caused restlessness characterised by bleating, groaning, grunting and limb movements that lasted for up to 5 min. This phenomenon has not been reported previously. This was followed by a period of calm and the animals remained sedated for 25 to 30 min. Over the same period of sedation, xylazine provided good muscle relaxation. Vocalisation and neck flexing following administration of xylazine in goats has been reported to occur[28]. Signs of sedation following administration of xylazine in goats include lowering of the head and neck, partial drooping of the upper eyelid, protrusion of the nictitating membrane and tongue, muscular incoordination and staggering gait[35]. Protrusion of the tongue following administration of xylazine to steers has also been reported[34]. While restrained in lateral recumbency, the goats displayed signs of sedation within 5 min of xylazine administration such as protrusion of the nictitating membrane and tongue, and drooping of the upper eyelids. The duration of sedation lasted for 25 to 30 min and recovery 68 to 74 min, which is in agreement with previous findings in the same species[19,32]. It has been shown that heifers injected with xylazine and exposed to heat-stress took significantly longer to rise from recumbency compared to those exposed to thermoneutral environmental conditions, and it

was suggested that this could be due to increased sensitivity to xylazine of animals in the heat-stress environment[15]. A similar reaction was not observed in goats in the present study following acute exposure to similar environmental conditions.

Intravenous injection of xylazine induces profuse salivation in ruminants[6]. In this study xylazine induced salivation, starting as small amounts, which proceeded to become copious. This was in agreement with reports in goats[23,28,30,35], cattle[15,34] and donkeys[27]. In the present study, salivation started as early as 5.7 ± 1.4 min and lasted for as long as 45.7 ± 2.1 min, and correlated well with previous findings[23,35]. Salivation after xylazine administration has been attributed to the inability of the goats to swallow during sedation[23]. In this study, there was no significant difference in the duration of salivation in the goats under different environmental conditions, contrary to findings in heifers. Salivation took longer to subside in heifers subjected to heat stress compared to those exposed to thermoneutral conditions, and it was suggested that heat-stresed animals were more sensitive to xylazine than those in thermoneutral conditions[15].

Xylazine provided good analgesia of abdominal and thoracic skin but no analgesia was present below the coronet. Xylazine has been reported to provide hardly any to moderate analgesic action in the region of the distal extremities[16,22,27]. In this study, xylazine provided good analgesia, in agreement with findings in goats[1,12,35], sheep[31] and cattle[15]. The analgesic property is probably due its action on the autonomic and central nervous system. Even when it is injected locally, xylazine has a potent analgesic effect[22]. The analgesia provided by xylazine is sometimes not adequate, as some animals reacted to surgical stimulation, even when supportive local or regional analgesia was used in combination with intravenous xylazine[34]. Xylazine should be supplemented with some form of effective analgesia whenever a surgical procedure is to be performed[34]. The analgesia provided by xylazine in goats in this study lasted for up to 44 min, which is longer than the times reported in sheep[31]. Differences in environmental conditions in this study did not have significant effects on duration of analgesia as has been observed in cattle[15]. The long duration of analgesia could be due to the greater sensitivity to xylazine of goats compared to sheep[12].

Longer recovery periods, longer duration of salivation and longer duration of analgesia in animals exposed to heat stress as compared to thermoneutral conditions has been attributed to increased sensitivity to xylazine in heat-stressed animals[15]. There is a possibility that hormonal or neural changes develop in heat-stressed animals, whereby their metabolic rate decreases as a result of decreased thyroid hormones, which might alter xylazine kinetic properties[43]. The differences between the results of this study and that of Fayed *et al.*[43] are possibly due to study design and or species differences. The heifers were conditioned to their respective environmental conditions for 35 days before the study, whereas the goats in this study were acutely exposed to the 3 different sets of environmental conditions without prior conditioning. Thyroid activity following acute exposure of cattle to 1 °C increases significantly from 36 h after exposure, whereas it remains depressed at 38 °C after 60 h following acute exposure[43]. In this study, the goats were exposed to the different environmental conditions for only 60 min, not long enough to alter thyroid activity and subsequently metabolic rate to effect a change in xylazine kinetic properties.

Urination after administration of xylazine is a common occurrence in goats[1,28,30]. In cattle, increased urine output lasts for up to 5 h, accompanied by the presence of glucose in the urine and increased urine pH, after administration of xylazine[40]. Not only the quantity of urine, but also the frequency of urination increases after xylazine administration in steers[34]. In this study, polyuria occurred after 21.0 ± 1.9 min and also after 69.6 ± 3.4 min. This is in agreement with previous reports in goats[1,28]. Polyuria observed in animals following administration of xylazine is attributed to hyperglycaemia and persists for up to 150 min in goats[28]. Alternatively, it could be secondary to the effects of xylazine on the formation or release of anti-diuretic hormone (ADH)[40]. Polyuria observed in goats in this study coincided with the period of hyperglycaemia, which started at 15 min post-xylazine injection, peaking at 30 min and persisting to the end of the 60-min monitoring period.

A significant reduction in MAP following administration of xylazine as observed in the present study has also been reported earlier in goats and other species[3,7,9,23]. The decrease in arterial blood pressure due to xylazine in goats is dose-related, and the magnitude of decrease in blood pressure depends on the route of administration of the drug[23]. Following intramuscular administration, xylazine may not significantly alter blood pressure despite the higher dose used[40], but greater responses in arterial blood pressure are achieved when the intravenous route is used, despite the smaller doses injected[23]. Intravenous administration of xylazine in this study resulted in an initial transient increase in MAP in all 3 environments. This phenomenon also occurs in sheep[9] and calves[3]. Following intravenous administration, α_2-agonists typically produce an initial rise in arterial blood pressure followed by a sustained decrease[8]. The initial short-lived pressor response has been reported to occur due to stimulation of the peripheral arterial postjunctional α_1 and α_2 adrenoceptors. The sustained hypotensive response has been attributed to central α_2 adrenoceptor stimulation[33].

Acute environmental changes did not result in significant changes in heart-rate after xylazine administration in the goats. However, at 14 °C the mean rate was significantly ($P < 0.05$) lower than baseline values. This could be attributed to hypothermia and decreased metabolic rate. A reduction in heart-rate following intramuscular or intravenous xylazine has been reported in goats[12,23,24,28,32,35], cattle[7,42], sheep[4,9] and horses[11,17]. Similar effects are seen when the drug is administered epidurally in goats[1] and cattle[38]. The reduction in heart-rate in goats is dose-dependent[23] and can remain depressed for up to 24 hours[12,28,32]. In addition to bradycardia, xylazine also caused an AV-block followed by tachycardia. It is not uncommon to have episodes of missed[4,5] and irregular heart-beats[1] accompanying bradycardia after xylazine administration in animals. In ponies, intravenous administration of xylazine results in sino-atrial (SA) blocks and transient AV-blocks within the 1st minute of its injection[17]. However, the authors were not certain whether the cause of the SA-block was due to baroreceptor reflex and/or vagotonic effects. It is suggested that xylazine causes a decrease in heart-rate *via* its central and peripheral suppression of the sympathetic system[24,33], or a physiological response to hypertension[10]. The ability of xylazine to decrease heart-rate has been attributed to the withdrawal of the sympathetic tone, and the direct depressant action on the cardiac pacemaker and conduction tissue[2,4,21,22,37].

Xylazine significantly reduced the ventilation rate in goats in the 14 °C environment compared to baseline rates, but no significant changes in rate could be ascribed to acute changes in environmental conditions. The above-mentioned decrease might be due to hypothermia and decreased metabolic rate. Xylazine is known to depress the ventilation rate[1,4,12,16,20,24,26,28,41], which can remain below baseline values for hours following its administration[28,32,35]. When injected epidurally, xylazine can cause a reduction

in the ventilation rate, and irregular breathing[1,38]. In this study, bradypnoea alternated with tachypnoea, dyspnoea and periodic apnoea followed by regular and deep breathing. This has been reported previously in goats and other species[4,5,23,35]. Apart from causing reduction in ventilation rate, a concurrent decrease in tidal volume in goats[28] and sheep[4] may occur. The effects of xylazine on pulmonary function have been attributed to its central α_2-adrenoreceptor-mediated activity, which results in respiratory depression[1,32].

Xylazine induced significant changes in haemoglobin concentration, red blood cell count, total white blood cell count, total protein, haematocrit, mean corpuscular volume, and mean corpuscular haemoglobin concentration in the goats in under the different environmental conditions. The observed decrease in total number of erythrocytes, leukocytes, haemoglobin concentration[12,24] and haematocrit[12,13,24], during the period of sedation following administration of xylazine has been reported in goats and other species. Contrary to other findings in goats[24], xylazine caused significant ($P < 0.05$) reduction in total plasma proteins in the goats exposed to 24 and 34 °C in this study. The haemolysis observed in plasma of blood samples collected in the first 5 min following injection of xylazine is in agreement with previous reports after propionylpromazine administration[13]. This lytic effect may contribute to the decline in packed cell volume[13]. Pooling of blood in the spleen as has been reported with other tranquillisers in goats[29] can also lead to decrease in red blood cell count, haematocrit and haemoglobin concentration following administration of xylazine hydrochloride. Engorgement of the spleen leads to a reduction in blood components in the peripheral circulation[36]. The fall can also be attributed to haemodilution caused by an influx of intestinal fluids due in part to the decreased heart-rate and to the low blood pressure[14]. The fall in total white cell count is probably the result of adrenocortical stimulation and the subsequent effect of glucocorticoids on circulating neutrophils and lymphocytes following xylazine injection. Increased adrenocortical activity causes depression of lymphocytic tissue and disappearance of lymphocytes from the peripheral blood[36].

In conclusion, the administration of xylazine to goats and exposing them to acute changes in environmental conditions resulted in significant changes in the measured ventilatory and cardiovascular variables, independent of the climatic changes.

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