Effects of xylazine on acid-base balance and arterial blood-gas tensions in goats under different environmental temperature and humidity conditions

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ABSTRACT

The effects of acute exposure to 3 different temperature and humidity conditions on arterial blood-gas and acid-base balance in goats were investigated after intravenous bolus administration of xylazine at a dose of 0.1 mg/kg. Significant ($P < 0.05$) changes in the variables occurred under all 3 environmental conditions. Decreases in pH, partial pressure of oxygen and oxyhaemoglobin saturation were observed, and the minimum values for oxygen tension and oxyhaemoglobin saturation were observed within 5 min of xylazine administration. The pH decreased to its minimum values between 5 and 15 min. Thereafter, the variables started to return towards baseline, but did not reach baseline values at the end of the 60 min observation period. Increases in the partial pressure of carbon dioxide, total carbon dioxide content, bicarbonate ion concentration, and the actual base excess were observed. The maximum increase in the carbon dioxide tension occurred within 5 min of xylazine administration. The increase in the actual base excess only became significant after 30 min in all 3 environments, and maximal increases were observed at 60 min. There were no significant differences between the variables in the 3 different environments. It was concluded that intravenous xylazine administration in goats resulted in significant changes in arterial blood-gas and acid-base balance that were associated with hypoxaemia and respiratory acidosis, followed by metabolic alkalosis that continued for the duration of the observation period. Acute exposure to different environmental temperature and humidity conditions after xylazine administration did not influence the changes in arterial blood-gas and acid-base balance.

Key words: acid-base, anaesthesia, blood-gas, goats, xylazine.

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INTRODUCTION

Xylazine is widely used in various animal species for its potent sedative, analgesic and myorelaxant properties[5]. Reported adverse effects of xylazine are hypoxaemia, carbon dioxide retention and acid-base disturbances[4–7,10,11,16,17,21]. The field use of xylazine often requires the administration of this agent to compromised animals exposed to acute changes in environmental conditions. Xylazine administered to heat-stressed heifers resulted in a prolonged action of xylazine[8]. It was speculated that the duration of the effect of xylazine might be altered during acute changes in environmental conditions, and therefore result in increased morbidity or mortality. The purpose of this study was therefore to evaluate the short term effects of xylazine in goats under different environmental temperature and humidity conditions.

MATERIALS AND METHODS

Six adult, clinically healthy, non-descript indigenous African breed, castrated male goats, weighing between 21.0 and 34.0 kg (mean 28.2 ± 1.0 SEM), were used in this study. They were housed indoors in individual crates in premises devoid of temperature and humidity control. At least 1 month before the commencement of the study, the carotid artery was relocated to a subcutaneous position in all the animals under halothane anaesthesia. 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 crossover design was used in this investigation. The effects of the drug on acid-base balance and arterial blood gas tension were repeatedly examined during low, medium and high temperature and humidity exposure phases. A washout period of at least 7 days was allowed between phases. The first phase 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 %. Temperature and humidity control was set 12 h before each phase of the investigation to ensure uniformity of conditions in the room. Before the investigation, the goats were starved for 24 h and water was withheld for 12 h. The goats were weighed, restrained in lateral recumbency and the jugular grooves bilaterally surgically prepared for percutaneous venipuncture of the left jugular vein with a 18G catheter (Jelco®, Critikon) for drug administration. The relocated carotid artery on the right side was catheterised with a 20G catheter (Medican®, Medical Specialities) for arterial blood collection. Both catheters were flushed with heparinised saline, capped and sutured to the skin with No. 2/0 nylon (Ethicon). The animals were then transferred to the temperature- and humidity-controlled room, and maintained in lateral recumbency. An oesophageal thermometer probe from a multi-parameter physiological monitor (Propaq® 104EL, Protocol Systems, Oregon) was nasally introduced with the tip in the distal third of the oesophagus. After a stabilisation period of 10 min, xylazine hydrochloride (Rompun®, Bayer Animal Health, Isando) was injected intravenously as a bolus at a dose of 0.1 mg/kg body mass. Arterial blood samples (2 mℓ) were anaerobically collected from the carotid artery into 2.5 mℓ heparinised syringes and stored in iced water for analysis within 2 h of collection with a blood-gas analyser (Radiometer ABL 300, Copenhagen, Denmark). The samples were corrected for

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Table 1: **Mean** (±SEM) **of arterial blood-gas tensions and acid-base balance in goats following intravenous xylazine at a dose of 0.1 mg/kg, under 3 different environmental temperature and humidity conditions.**

Time (min)	Environment	pH[a]	PaO_2[b]	$PaCO_2$[c]	O_2SAT[d]	$[HCO_3^-]$[e]	Total CO_2[f]	ABE[g]
0	14 °C	7.39 (0.01)	10.7 (0.6)	4.9 (0.2)	93.2 (1.0)	21.3 (0.7)	22.3 (0.8)	–2.2 (0.7)
5		7.34 (0.01)*	4.0 (0.4)*	5.9 (0.3)*	43.5 (6.3)*	22.4 (0.8)	23.6 (0.8)*	–2.3 (0.7)
15		7.35 (0.01)	5.2 (0.5)*	5.9 (0.3)*	62.3 (6.0)*	23.1 (0.7)*	24.4 (0.7)*	–1.6 (0.6)
30		7.37 (0.01)	5.8 (0.5)*	5.7 (0.2)*	71.5 (5.2)*	24.0 (0.8)*	25.2 (0.8)*	–0.5 (0.7)
60		7.43 (0.01)	6.9 (0.5)*	5.2 (0.2)	84.2 (2.5)	25.2 (1.0)*	26.3 (1.0)*	1.4 (0.9)*
0	24 °C	7.39 (0.01)	10.5 (0.5)	4.9 (0.1)	92.9 (2.5)	20.7 (0.6)	21.7 (0.6)	–2.9 (0.6)
5		7.33 (0.01)*	4.0 (0.4)*	6.3 (0.2)*	43.5 (5.6)*	22.5 (0.5)*	23.5 (0.6)	–2.6 (0.5)
15		7.33 (0.01)*	4.8 (0.5)*	6.2 (0.2)*	56.1 (6.4)*	23.4 (0.7)*	24.6 (0.7)*	–1.8 (0.6)
30		7.38 (0.01)	5.7 (0.4)*	5.8 (0.3)*	71.0 (4.0)*	24.5 (0.8)*	25.7 (0.9)*	0.1 (0.5)*
60		7.41 (0.01)	8.2 (0.8)*	5.5 (0.1)	86.5 (3.3)	25.3 (1.1)*	26.5 (1.1)*	1.5 (1.0)*
0	34 °C	7.40 (0.01)	10.0 (0.2)	5.0 (0.1)	92.6 (0.8)	22.0 (0.3)	23.0 (0.3)	–1.4 (0.3)
5		7.35 (0.01)*	4.0 (0.6)*	6.1 (0.1)*	42.0 (8.8)*	24.1 (0.5)*	25.3 (0.5)*	–0.6 (0.6)
15		7.36 (0.01)*	4.9 (0.6)*	6.0 (1.4)*	56.6 (7.2)*	24.3 (0.6)*	25.6 (0.7)*	–0.3 (0.7)
30		7.39 (0.01)	5.6 (0.5)*	5.9 (0.1)*	68.4 (5.0)*	25.7 (0.7)*	26.9 (0.7)*	1.5 (0.8)*
60		7.41 (0.01)	8.3 (1.0)*	5.2 (0.1)	85.5 (3.2)	25.0 (0.8)	26.1 (0.8)*	1.8 (0.8)*

[a]pH units.
[b]PaO_2 = arterial partial pressure of oxygen (kPa).
[c]$PaCO_2$ = arterial partial pressure of carbon dioxide (kPa).
[d]O_2SAT = oxyhaemoglobin saturation (%).
[e]$[HCO_3^-]$ = bicarbonate ion concentration (mmol/ℓ).
[f]Total CO_2 = total carbon dioxide content (mmol/ℓ).
[g]ABE = actual base excess (mmol/ℓ).
*Significantly different ($P < 0.05$) from baseline (time 0 min).

body temperature. The samples were collected at 'time zero' (baseline) and 5, 15, 30, 45, and 60 min post-xylazine injection. The blood was analysed for pH, arterial partial pressures of oxygen (PaO_2) and carbon dioxide ($PaCO_2$), oxyhaemoglobin saturation (SAT), bicarbonate ion concentration $[HCO_3^-]$, actual base excess (ABE) and total carbon dioxide content (TCO_2).

Data analysis

The data in these studies were analysed on a personal computer equipped with statistical software (SigmaStat 2.0, Jandel Corporation, San Rafael). Results are presented as mean and standard error of the mean (±SEM). To test for significance of difference over time as well as for differences between groups, data collected over time were analysed using a 2-way repeated measures analysis of variance. When a significant change was observed, comparisons between treatments were performed using a 1-way analysis of variance for repeated measures, followed by Bonferroni's test applied to examine for least significant differences. To test for significant changes with time within a group, a 1-way analysis of variance for repeated measures was applied followed by Bonferroni's test if significant changes were found. Where the data were either not normally distributed or the equal variance test failed, the data were analysed using Friedman repeated measures analysis of variance on ranks followed by Dunnett's method to examine deviations from baseline or 'time zero' (control) values. $P < 0.05$ was considered significant.

RESULTS

The results of the mean (±SEM) arterial blood-gas tensions and acid-base balance variables of the goats under the different environmental conditions are summarised in Table 1. Intravenous administration of xylazine resulted in a transient period of grunting, limb paddling, irregular breathing, and brief periods of apnoea. Cyanosis of the oral mucous membrane was observed in all animals. This was followed by a period of deep sedation. The effects on cardiopulmonary function and changes in body temperature have been reported in full[14]. Body temperature increased in the 34 °C environment with a maximum of 0.5 °C, and decreased in the 14 and 24 °C environments with a maximum decrease of 1.5 °C in the 14 °C environment[14].

Xylazine caused statistically significant ($P < 0.05$) changes in pH, PaO_2, SAT, $PaCO_2$, TCO_2, $[HCO_3^-]$, and SBE within 5 min of administration, except for the $[HCO_3^-]$ in the 14 °C environment, TCO_2, at the 24 °C environment, and the ABE in all 3 environments. The maximum decrease in PaO_2 and SAT occurred within 5 min of xylazine administration. The PaO_2 decreased to 4.0 (0.4) kPa in the 14 °C environment and the SAT to values between 42 (8.8) and 43.5 (6.3) % under the 3 environmental temperatures. The PaO_2 and the calculated acid-base variables, SBE and TCO_2, remained significantly different from baseline in all 3 environments at the end of the 60 min observation period.

DISCUSSION

Acute changes in environmental temperature and humidity conditions did not effect arterial blood-gas and acid-base variables in xylazine-treated goats. However, significant ($P < 0.05$) changes in arterial blood-gas tensions and acid-base balance (Table 1) were observed under all 3 sets of environmental conditions. The administration of xylazine was also associated with deep sedation, and changes in cardiopulmonary function[15] and body temperature[14].

The changes in arterial blood-gas and acid-base balance variables observed in this investigation were in agreement with changes previously reported in cattle[2,6,20], goats[10,11] and sheep[3,4]. The time of maximal change (after 5 min) was somewhat shorter compared to the previously reported times of maximal change around 10–15 min. This was probably the result of intravenous administration and the higher dose (0.1 mg/kg) used for xylazine in this investigation. The acute decreases in the $PaCO_2$, PaO_2, SAT and cyanosis were probably the result of the effects of xylazine on cardiopulmonary function[15]. Arterial hypoxaemia associated with minimum oxygen tensions of 4 kPa under all 3 environmental conditions were in agreement with the reported oxygen tensions in sheep of

4.3 kPa[4]. Hypoxaemia was also reported in other species[5,7,8,13]. The hypoxaemia observed in this investigation was independent of environmental conditions and probably partly the result of hypoventilation due to central respiratory depressant effects of the drug[1,20]. Changes in breathing such as bradypnoea, tachypnoea, forced breathing and apnoea as observed in this investigation have been reported previously[4,9,21]. A decrease in tidal volume has also been reported in goats[13]. Restraint in lateral recumbency might also have contributed to the changes observed in this investigation. It has been reported in cattle that restraint contributes to similar changes as a result of ventilation-perfusion mismatch, although there is a large difference in body size compared to goats[6]. Changes in pulmonary function associated with changes in transpulmonary pressure as a result of partial upper respiratory tract obstruction were reported in sheep after xylazine administration. It has been suggested that these changes were the result of α_2-adrenoceptor-mediated activity[4,20]. Decreases in arterial oxygen tension, haemoglobin saturation, and packed cell volume in compromised animals with anaemia may have an unfavourable effect on peripheral oxygen delivery, especially if associated with decreases in cardiac output and arterial blood pressure[6,19]. This may result in increased morbidity or mortality in animals.

Arterial pH decreased below baseline within 5 min of xylazine administration as result of an increased $PaCO_2$ (respiratory acidosis). The $PaCO_2$ started to improve towards baseline after 30 min, probably as result of recovery from xylazine. However, both $PaCO_2$ and the total CO_2 remained above baseline. Increases in $[HCO_3^-]$ above baseline occurred over the observation period, and resulted in metabolic alkalosis. The arterial pH was increased above baseline values at 60 min for all 3 sets of environmental conditions despite the $PaCO_2$ and total CO_2 that were above baseline. The metabolic alkalosis is in agreement with a previous report in goats, although the magnitude of the alkalosis was higher, with a pH of approximately 7.48 and a BE of 5 mmol/ℓ after administration of intravenous medetomidine[18]. The 60 min observation period used in this investigation may not be optimal for the detection of maximal changes in acid-base variables.

The changes in the acid-base balance and blood-gas tensions observed in this investigation were independent of changes in environmental temperature and humidity conditions. The prolonged action of xylazine in heifers in an environment conducive to heat stress was observed after prolonged exposure to increased ambient temperature. It has been suggested that long-term metabolic changes such as decreased thyroid function and metabolic rate may result in the altered clinical effects of xylazine[8,12]. In comparison, the goats in this investigation were exposed to acute changes in the environment, which would not permit metabolic or hormonal changes, and could explain the reason for not observing similar changes in the response to xylazine.

In conclusion, intravenous xylazine in goats exposed to acute changes in environmental temperature and humidity conditions resulted in hypoxaemia, respiratory acidosis, and compensatory metabolic alkalosis. The changes were statistically significant under all 3 sets of environmental conditions, but no significant differences were observed between the different environments.

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