Sedative and cardiopulmonary effects of acepromazine, midazolam, butorphanol, acepromazine-butorphanol and midazolam-butorphanol on propofol anaesthesia in goats

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ABSTRACT

The sedative, propofol-sparing and cardiopulmonary effects of acepromazine, midazolam, butorphanol and combinations of butorphanol with acepromazine or midazolam in goats were evaluated. Six healthy Boer – Indigenous African crossbreed goats were by randomised cross-over designated to 6 groups: Group SAL that received saline, Group ACE that received acepromazine, Group MID that received midazolam, Group BUT that received butorphanol, Group ACEBUT that received acepromazine and butorphanol and Group MIDBUT that received midazolam and butorphanol as premedication agents intramuscularly on different occasions at least 3 weeks apart. The degree of sedation was assessed 20 minutes after administration of the premedication agents. Thirty minutes after premedication, the dose of propofol required for induction of anaesthesia adequate to allow placement of an endotracheal tube was determined. Cardiovascular, respiratory and arterial blood-gas parameters were assessed up to 30 minutes after induction of general anaesthesia. Acepromazine and midazolam produced significant sedation when administered alone, but premedication regimens incorporating butorphanol produced inconsistent results. The dose of propofol required for induction of anaesthesia was significantly reduced in goats that received midazolam alone, or midazolam combined with either acepromazine or butorphanol. The quality of induction of anaesthesia was good in all groups, including the control group. Cardiovascular , respiratory and blood-gas parameters were within normal limits in all groups and not significantly different between or within all groups. In conclusion: sedation with midazolam alone, or midazolam combined with either acepromazine or butorphanol significantly reduces the induction dose of propofol with minimal cardiopulmonary effects in goats.

Key words: acepromazine, anaesthesia, butorphanol, goat, midazolam, propofol, sedative.

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INTRODUCTION

The concept of administering sedatives before an injectable anaesthetic induction agent is well accepted in veterinary practice. Sedatives are used pre-operatively to induce sedation, improve the quality of induction of anesthesia and more importantly, may result in fewer drug-related adverse effects by reducing the amount of injectable or inhalation anaesthetics required to induce and maintain general anesthesia[17,21,29].

Sedatives used for calming small ruminants include α_2 adrenoceptor agonists like xylazine, phenothiazines like acepromazine, benzodiazepines like diazepam and midazolam, and opioids like butorphanol[28].

Xylazine is a commonly used sedative in ruminants[11,12,32] but there are concerns about the threat of hypoxaemia associated with its use in small ruminants[2,10,18].

Development of profound hypoxaemia in goats and sheep probably as a result of pulmonary oedema and extravasation of red blood cells into the alveoli has been documented especially with α_2 adrenoceptor agonists such as xylazine, romifidine, detomidine and medetomidine[2,10,18,23]. This development of hypoxaemia has been documented in sheep following administration of all 4 α_2 adrenoceptor agonists listed above[10,13,24], but in goats, has only been documented following administration of xylazine[18]. Some authors still recommend cautious use of medetomidine, but only in young healthy goats[7]. This study did not include assessment of the α_2 adrenoceptor agonists due to the uncertainty about their safety when used in goats.

Acepromazine (ACP) is the most commonly used phenothiazine derivative for mild tranquillisation in veterinary practice[3,16]. Phenothiazines have antagonistic action on dopamine receptors, as well as on histamine receptors, serotonin receptors and catecholamine receptors[14,21]. Acepromazine produces numerous effects such as peripheral vasodilation, hypotension, hypothermia and behavioural modifications[16]. Acepromazine is commonly combined with opioids as it lacks analgesic properties[16,21].

Midazolam is a water-soluble benzodiazepine that is considered to be fast-acting with a short elimination half-life[5,21]. It can, unlike diazepam, be administered by the intramuscular route as well as the intravenous route[21]. Midazolam has mild cardiovascular and respiratory effects and is commonly used as a mild tranquilliser, a muscle relaxant and anticonvulsant[21]. Benzodiazepines have agonistic effects on specific benzodiazepine receptors located in the postsynaptic nerve endings within the central nervous system[5,22]. The resultant increase in availability of the inhibitory neurotransmitter glycine leads to the anxiolytic and muscle relaxant effects. Sedation and anticonvulsant activity are mediated by gamma-aminobutyric acid (GABA) in the cerebral cortex and motor centres[35]. The sedative and hypnotic effects of midazolam are dose-dependent as well as dependent on route of administration. Midazolam can produce maximal sedative effects in 20 minutes after intramuscular administration of 0.6 mg/kg[33].

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Table 1: **Profile of the goats (**mean ± standard deviation) **used in this study where preanaesthetic administration of saline 1.0 mℓ** (SAL group)**, acepromazine 0.05 mg/kg** (ACE group)**, midazolam 0.3 mg/kg** (MID group)**, butorphanol 0.1 mg/kg** (BUT group)**, acepromazine 0.05 mg/kg with butorphanol 0.1 mg/kg** (ACEBUT group)**, and midazolam 0.3 mg/kg with butorphanol 0.1 mg/kg** (MIDBUT group) **was followed by intravenous administration of propofol for induction of general anaesthesia in goats.**

Group	Variable						
	Group size	Age (months)	Weight (kg)	TSP (g/ℓ)	Haematocrit (ℓ/ℓ)	White cell count ($\times 10^9$/ℓ)	Temperature (°C)
SAL	6 (3 male, 3 female)	6.2 ± 2.1	23.3 ± 4.2	61.3 ± 3.9	0.34 ± 0.04	13.8 ± 2.7	39.0 ± 0.4
ACE	6 (3 male, 3 female)	6.3 ± 1.9	21.9 ± 4.3	61.2 ± 6.9	0.31 ± 0.06	15.1 ± 4.7	39.0 ± 0.6
MID	6 (3 male, 3 female)	6.2 ± 1.8	23.3 ± 4.4	61.7 ± 3.5	0.32 ± 0.06	13.0 ± 1.5	39.1 ± 0.4
BUT	6 (3 male, 3 female)	7.7 ± 1.6	23.0 ± 3.7	63.8 ± 5.7	0.30 ± 0.05	13.6 ± 2.2	39.1 ± 0.6
ACEBUT	6 (3 male, 3 female)	7.8 ± 1.7	22.8 ± 3.5	63.4 ± 6.9	0.36 ± 0.09	17.9 ± 7.0	39.0 ± 0.8
MIDBUT	6 (3 male, 3 female)	6.3 ± 1.8	23.2 ± 4.6	62.3 ± 0.6	0.32 ± 0.04	15.3 ± 2.9	38.9 ± 0.3
		NS	NS	NS	NS	NS	NS

NS: no significant differences ($P < 0.05$) between the 6 groups.

Butorphanol, a synthetic opioid, is an agonist at κ-opioid receptors and an antagonist at μ-opioid receptors[8,19,34]. There are conflicting statements in the literature on effects of butorphanol on μ-opioid receptors as some authors claim it is a partial agonist[14]. Opioids are traditionally included in balanced anaesthesia protocols for their analgesic effects, but they also have sedative effects[21]. Butorphanol has analgesic properties in ruminants, however, it can also induce excitatory behavioural changes[6,14]. Butorphanol at a dose of 0.02–0.50 mg/kg, administered intramuscularly or intravenously, increases sedation from acepromazine or benzodiazepines[16,28,34], while at the same time the sedatives (acepromazine and benzodiazepines) would help diminish the behavioural effects of butorphanol[6].

Propofol (2,6-diisopropyl-phenol) is one of the induction agents commonly used in goats. It has a rapid and smooth onset of action and is cleared rapidly from the tissues[15,20,27]. Besides metabolism by the liver, extrahepatic sites of metabolism, most prominently the lung, have been claimed for propofol[15]. Propofol causes a dose-related decrease in blood pressure due to peripheral vasodilation and myocardial depression, bradycardia, epileptiform seizures and true convulsions[4,30]. When administered at a dose of 4–7 mg/kg intravenously in unpremedicated goats and sheep, propofol will induce sufficient anaesthesia for endotracheal intubation[25,27], while 3 mg/kg was shown to be sufficient for endotracheal intubation in premedicated goats[3]. One pharmacokinetic study of propofol in goats showed the half-life of propofol to be 15.5 minutes[27].

The purpose of this study was to determine the quality of sedation, the magnitude of reduction of induction dose of propofol and the quality of general anaesthesia obtained after sedation of goats with acepromazine, midazolam and butorphanol and combinations of butorphanol with acepromazine or midazolam. The impact of these anaesthesia protocols on the cardiovascular and respiratory systems as assessed by such parameters like heart rate, blood pressure, respiratory rate and blood-gas tensions were also assessed.

MATERIALS AND METHODS

Experimental design and instrumentation

A day before the investigations, the goats, which were housed at the Onderstepoort Teaching Animal Unit (OTAU), were transferred to the University of Pretoria Biomedical Centre (UPBRC) where the studies were carried out. Six clinically healthy Boer–Indigenous African crossbreed goats were used in this study (Table 1).

Using a table of random numbers, the goats were assigned, in a randomised cross-over design with a 3-week interval between treatments, to 6 groups as follows: Group SAL that received saline (0.9 % NaCl) as a premedication agent, Group ACE that received acepromazine as a premedication agent, Group MID that received midazolam as a premedication agent, Group BUT that received butorphanol as a premedication agent, Group ACEBUT that received acepromazine and butorphanol as premedication agents and Group MIDBUT that received midazolam and butorphanol as premedication agents.

Food and water were withheld overnight, approximately 18–24 hours before anaesthesia. A clinical examination of the goats was done a day before anesthesia. Venous blood samples in ethylenediaminetetraacetic acid (EDTA) tubes (BD Vacutainer® Systems, Plymouth, United Kingdom) for a complete blood count and in serum tubes (BD Vacutainer® Systems) for serum protein analysis were collected soon after completion of physical examination of the goats.

The goats were weighed using an electronic scale (Jadever® Richter Scale, Jadever, Scale Co. Ltd, Taipei, Taiwan) the morning of treatment day. The goats were placed on a custom-made sling-cum-table to make restraint easier throughout the duration of the investigations. The auricular artery was percutanously catheterised using a 24-gauge catheter (Jelco®, Medex Medical Ltd, Rossendale, Great Britain) for measurement of arterial blood pressure and collection of arterial blood samples for blood-gas analysis. A transducer (DTX Plus™ disposable transducer, BD Medical, Johannesburg, South Africa) and a multi-parameter monitor (Model BSM-4103K, Nihon Kohden Corporation, Tokyo, Japan) calibrated according to manufacturer recommendations were used for blood pressure measurements. The scapulohumeral joint and the point of the sternum were taken as the zero reference points for arterial blood pressure measurements in upright and recumbent goats, respectively. Electrocardiography electrodes were attached to the same multi-parameter monitor so that an electrocardiogram (ECG) could be monitored. An 18-gauge catheter (Introcan® Safety, B. Braun Medical Incorporated, Bethlehem, United States of America) was introduced into the cephalic vein for administration of intravenous propofol and fluids.

The goats were then premedicated by the intramuscular route with 1 mℓ of saline (Intramed Sodium Chloride 0.9 %® Fresenius, Bodene, trading as Intramed, Port Elizabeth, South Africa) (Group SAL), acepromazine maleate (Aceprom 2®, Bayer, Isando, South Africa) at 0.05 mg/kg (Group ACE), midazolam (Dormicum®, Roche Products, Isando, South Africa) at 0.3 mg/kg (Group MID), butorphanol tartrate (Torbugesic®, Fort Dodge Animal Health, Fort Dodge, USA) at 0.1 mg/kg (Group BUT), acepromazine maleate at 0.05 mg/kg and butorphanol tartrate at 0.1 mg/kg (Group ACEBUT), or

Table 2: **Scoring system used to evaluate the degree of sedation, quality of induction of anaesthesia and quality of recovery from anaesthesia in goats used in this study where preanaesthetic administration of saline 1.0 mℓ** (SAL group)**, acepromazine 0.05 mg/kg** (ACE group)**, midazolam 0.3 mg/kg** (MID group)**, butorphanol 0.1 mg/kg** (BUT group)**, acepromazine 0.05 mg/kg with butorphanol 0.1 mg/kg** (ACEBUT group)**, and midazolam 0.3 mg/kg with butorphanol 0.1 mg/kg** (MIDBUT group) **was followed by intravenous administration of propofol for induction of general anaesthesia in goats.**

Score	Sedation (0–3)	Induction of anaesthesia (0–2)	Recovery from anaesthesia (0–2)
0	No sedation	Poor (excitement, jumps or attempt to stand after becoming recumbent, unable to place endotracheal tube)	Poor (restless)
1	Mild sedation (mild sensory or motor deficits)	Fair (slightly prolonged (>2 minutes) induction time or mild excitation)	Fair (relatively smooth with some restless)
2	Moderate sedation (may assume sternal recumbency)	Good (smooth induction, no excitement, endotracheal intubation easy)	Good (smooth)
3	Severe sedation (failing to maintain sternal recumbency, but may raise the head without holding it up)		

midazolam 0.3 mg/kg and butorphanol 0.1 mg/kg (Group MIDBUT).

The degree of sedation was scored 20 minutes after administration of the premedication agent (Table 2), as it is most probable that the sedative effects were optimum at this time.

Thirty minutes after administration of the premedication agents, propofol (Propofol 1 %® Fresenius, Bodene, trading as Intramed, Port Elizabeth, South Africa) was administered intravenously to induce a level of anaesthesia adequate to allow placement of an endotracheal tube. A quarter of the estimated total dose (10 mg/kg) of propofol necessary to induce anaesthesia was administered within 30 seconds. A tenth of the estimated total dose of propofol was then administered intermittently, checking depth of anaesthesia between administrations, until the jaws were adequately relaxed to allow intubation. Placement of the endotracheal tube (silicone tube, internal diameter 7.5 mm) was done with the goats in sternal recumbency using a laryngoscope to facilitate the process. Immediately after intubation, the goats were placed in left lateral recumbency and the total dose of propofol required for induction was recorded. Quality of induction was scored at this point (Table 2).

The goats were allowed to recover after intubation and no other anaesthetic agents were administered thereafter. They were allowed to breathe room air spontaneously. Ringer Lactate solution (Intramed Ringer-Lactate® Fresenius, Bodene, trading as Intramed, Port Elizabeth, South Africa) was administered at a rate of 4 mℓ/kg/h intravenously up to 30 minutes after induction of general anaesthesia. The endotracheal tube was removed after the goats regained the swallowing reflex. Time to extubation and sternal position were recorded. It was noted whether the goats were able to walk voluntarily by the time they were taken off the working table (*i.e.* at 30 minutes after induction of general anaesthesia). Times to extubation and sternal position were determined as the interval between the time the last dose of propofol was administered and the time a particular event happened. Quality of recovery was scored once the goats were able to walk voluntarily (Table 2).

Cardiopulmonary parameters like systolic, diastolic and mean arterial pressures, heart rate and respiratory rate as well as body temperature were recorded at the following times: prior to administration of the premedication agents (baseline), 20 minutes after administration of the premedication agents, at induction and at 10, 20 and 30 minutes after induction. Arterial blood samples for blood-gas analysis were collected in pre-heparinised (Heparin sodium – Fresenius 1000 i.u/mℓ, Bodene, trading as Intramed, Port Elizabeth, South Africa) plastic syringes (Omnifix® 1 mℓ, B. Braun, Melsungen, Germany) at the following times: prior to premedication, 20 minutes after premedication and 20 minutes after intubation. The syringes containing arterial blood samples were sealed and placed in ice water for blood-gas analysis within 1 hour of collection. From these blood samples, arterial oxygen tension (PaO_2), arterial carbon dioxide tension ($PaCO_2$), arterial hydrogen ion concentration (pHa), arterial bicarbonate ion ($[HCO_3^-]$) concentration and arterial oxygen tension (SaO_2) were measured and recorded. Blood gas analysis was done using a pre-calibrated machine (Rapidlab™ 348 pH/Blood Gas and Electrolyte Analyser, Siemens Medical Solutions Diagnostics, Midrand, South Africa).

This study was approved by both the Animal Use and Care Committee and the Research Committee of University of Pretoria's Faculty of Veterinary Science.

Statistical analysis

Data on physiological parameters, induction dose as well as time to extubation and sternal position are reported as mean ± S.D. Medians and ranges are reported for scores (sedation, induction and recovery). Systolic, diastolic and mean arterial pressures, heart rate, respiratory rate, PaO_2, $PaCO_2$, pH, bicarbonate concentration, SaO_2 and body temperature data were tested for normality in distribution using the Shapiro-Wilks test and found to be distributed normally . The data were then analysed for statistically significant differences between and within groups using a repeated measures analysis of variance test. For the scores (sedation, induction and recovery), induction dose, as well as time to extubation and sternal recumbency, the Friedman rank sum test adjusted for ties was used to test differences between groups. Where statistically significant differences between groups were observed, a pair-wise Wilcoxon test and a Bonferroni adjustment for multiple testing was used to identify which groups were different. A value of $P < 0.05$ was considered significant. The data were analysed using the R® statistical software, Version 2.7.2 (The R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

There were no statistically significant differences between the groups, either in

Table 3: **General anesthesia induction dose, extubation time, sternal position time** (mean ± standard deviation)**, percentage reduction in induction dose, and sedation score, induction score, recovery score** [median(range)] **following preanaesthetic administration of saline 1.0mℓ** (SAL group)**, acepromazine 0.05 mg/kg** (ACE group)**, midazolam 0.3 mg/kg** (MID group)**, butorphanol 0.1 mg/kg** (BUT group)**, acepromazine 0.05 mg/kg with butorphanol 0.1 mg/kg** (ACEBUT group)**, and midazolam 0.3 mg/kg with butorphanol 0.1 mg/kg** (MIDBUT group) **and then intravenous administration of propofol for induction of general anaesthesia in goats.**

Group	Variable						
	Induction dose propofol (mg/kg)	**Reduction in induction dose** (%)	**Sedation score**	**Induction score**	**Extubation time** (min)	**Sternal position time** (min)	**Recovery score**
SAL	5.3 ± 1.0	0.0	0(0–0)	1(0–2)	2.5 ± 1.2	4.0 ± 0.1	2(1–2)
ACE	4.2 ± 0.9	20.1	1.5(1–2)*	2(1–2)	5.2 ± 2.9	8.0 ± 4.0	2(2–2)
MID	3.2 ± 0.3*	39.7*	2(1–2)*	2(2–2)	6.5 ± 2.1	9.7 ± 3.4	2(1–2)
BUT	4.1 ± 0.4	22.1	1(0–2)	2(1–2)	4.2 ± 1.6	7.0 ± 2.4	2(2–2)
ACEBUT	3.8 ± 0.4*	27.8*	1.5(0–2)	2(2–2)	6.5 ± 2.9	8.5 ± 2.8	2(2–2)
MIDBUT	3.3 ± 0.6*	38.1*	1(0–3)	2(2–2)	8.8 ± 2.3	13.7 ± 4.8	2(2–2)
	#	#	#	#	#	#	NS

#, Significant differences ($P < 0.05$) between the 6 groups, NS: no significant differences ($P < 0.05$) between the 6 groups.
*Significantly different ($P < 0.05$) from SAL (control) group.

terms of age and weight or between pre-anaesthetic total serum protein, haematocrit, white cell count and body temperature (Table 1).

Statistically significant differences were present among the 6 groups in terms of sedation score ($P = 0.013$), propofol induction dose ($P = 0.006$), extubation time ($P = 0.005$) and sternal position attainment time ($P = 0.005$), but no statistically significant differences among the 6 groups were noted in score for quality of anaesthesia recovery. Pair-wise comparisons showed that the induction doses in the MID group ($P = 0.032$), ACEBUT group ($P = 0.032$) and MIDBUT group ($P = 0.032$) were significantly lower than the induction dose in the control group. The sedation scores were significantly higher in the ACE group ($P = 0.035$) and MID group ($P = 0.033$) in comparison with the control group. Pair-wise comparison of induction scores, extubation times and sternal position attainment times did not show any statistically significant differences between the control group and any of the treatment groups (Table 3, Fig. 1).

Cardiovascular system variables did not show any statistically significant differences between the control group and any of the treatment groups as well as between the baseline reading and any other time point reading within a group (Table 4). The ECG did not show any arrhythymias for any of the sedative regimens.

Respiratory system variables were not statistically significantly different both within groups and when treatment groups were compared with the control group with the exception of 3 data points. In the MID group respiratory rate was significantly lower at 1 minute ($P = 0.0003$) after induction of anaesthesia compared with the baseline reading and in the ACEBUT group respiratory rate was significantly lower at 1 minute ($P = 0.000006$) and at 10 minutes ($P = 0.003$) after induction of anaesthesia compared with the baseline reading (Table 5).

Of the adverse effects observed; clonic-tonic convulsions and/or opisthotonus at induction were observed in 6 goats (1 SAL group, 2 ACE group, 1 MID group and 2 BUT group) while 1 goat from the SAL group showed excitement (characterised by vocalisation and falling around) at recovery, 1 goat each from the ACE group and MIDBUT group had induction apnoea lasting more than 30 seconds at induction and 1 goat from the ACEBUT group had ruminal bloat during recovery from anaesthesia.

All the goats were able to stand and walk voluntarily after 30 minutes of induction of anaesthesia.

DISCUSSION

Uniformity of distribution of the descriptive data of the goats among the groups is supported by the fact that there were no statistically significant differences in the signalment (age, weight) as well as pre-anaesthetic total serum protein, haematocrit, white cell count and body temperature. This was largely expected since a randomised crossover design was used in allocation of the goats to the groups.

Acepromazine and midazolam, in agreement with currently available literature, produced a significant degree of sedation when administered alone[3,33], but when combined with butorphanol the sedation score did not show any significant difference when compared with the unpremedicated goats. Butorphanol administered alone did not show a consistent significant degree of sedation. Lack of improvement in degree of sedation when butorphanol is combined with either acepromazine or midazolam is in disagreement with some studies in which a positive interaction was observed[16,34]. This could be due to numerous reasons, such as that the sample size and the scale used

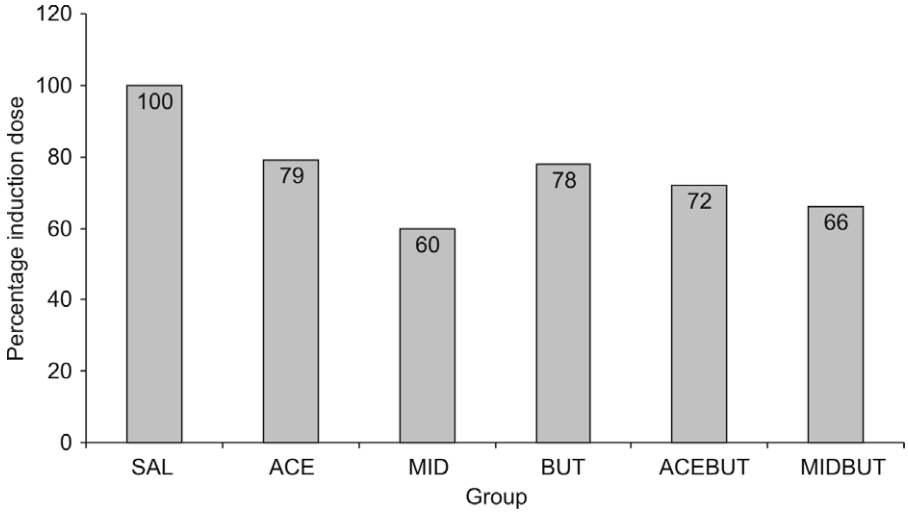

Fig. 1: **Propofol dose as percentage of dose required in the control group** (SAL) **after administration of acepromazine** (ACE), **midazolam** (MID)**and butorphanol** (BUT) **as well as combinations of butorphanol with acepromazine** (ACEBUT) **or midazolam** (MIDBUT) **in goats.**

Table 4: **Cardiovascular variables and body temperature** (mean ± standard deviation) **following preanaesthetic administration of saline 1.0 mℓ** (SAL group)**, acepromazine 0.05 mg/kg** (ACE group)**, midazolam 0.3 mg/kg** (MID group)**, butorphanol 0.1 mg/kg** (BUT group)**, acepromazine 0.05 mg/kg with butorphanol 0.1 mg/kg** (ACEBUT group)**, and midazolam 0.3 mg/kg with butorphanol 0.1 mg/kg** (MIDBUT group) **and then intravenous administration of propofol for induction of general anaesthesia in goats.**

Variable	Group	Baseline	20 minutes post-sedation	Time after induction (minutes)			
				1	10	20	30
Heart rate (beats/minute)	SAL	86 ± 17	83 ± 12	122 ± 16	111 ± 28	96 ± 22	99 ± 13
	ACE	101 ± 26	97 ± 18	114 ± 10	107 ± 20	96 ± 14	99 ± 8
	MID	94 ± 15	86 ± 21	114 ± 21	105 ± 13	101 ± 12	100 ± 17
	BUT	82 ± 7	76 ± 13	117 ± 6	102 ± 28	89 ± 20	82 ± 16
	ACEBUT	105 ± 31	96 ± 23	117 ± 33	101 ± 32	104 ± 34	104 ± 27
	MIDBUT	84 ± 8	89 ± 18	120 ± 28	108 ± 10	94 ± 14	91 ± 8
Systolic blood pressure (mmHg)	SAL	120 ± 9	118 ± 13	124 ± 16	109 ± 9	107 ± 8	
	ACE	119 ± 31	98 ± 7	101 ± 25	99 ± 6	98 ± 8	
	MID	121 ± 11	110 ± 9	122 ± 34	121 ± 22	111 ± 12	
	BUT	112 ± 9	103 ± 10	104 ± 18	106 ± 12	100 ± 12	
	ACEBUT	122 ± 16	105 ± 8	96 ± 9	102 ± 11	104 ± 7	
	MIDBUT	115 ± 9	98 ± 7	100 ± 9	109 ± 15	105 ± 9	
Diastolic blood pressure (mmHg)	SAL	82 ± 5	82 ± 4	92 ± 14	80 ± 15	77 ± 9	
	ACE	74 ± 20	56 ± 11	59 ± 7	68 ± 12	62 ± 12	
	MID	79 ± 10	76 ± 13	86 ± 37	94 ± 33	83 ± 23	
	BUT	70 ± 11	69 ± 8	79 ± 18	82 ± 8	76 ± 13	
	ACEBUT	83 ± 18	68 ± 6	62 ± 14	75 ± 17	70 ± 13	
	MIDBUT	82 ± 11	66 ± 7	70 ± 14	77 ± 21	73 ± 14	
Mean arterial blood pressure (mmHg)	SAL	101 ± 5	95 ± 18	99 ± 22	92 ± 12	91 ± 9	
	ACE	94 ± 24	75 ± 11	79 ± 13	81 ± 9	77 ± 11	
	MID	98 ± 11	94 ± 15	104 ± 35	103 ± 26	93 ± 15	
	BUT	92 ± 6	87 ± 9	91 ± 18	93 ± 9	89 ± 12	
	ACEBUT	102 ± 16	86 ± 8	73 ± 15	86 ± 16	86 ± 10	
	MIDBUT	97 ± 11	80 ± 9	80 ± 14	88 ± 20	85 ± 14	
Body temperature (°C)	SAL	39.0 ± 0.4	39.4 ± 0.3	39.2 ± 0.3	39.2 ± 0.3	39.1 ± 0.4	39.1 ± 0.3
	ACE	39.0 ± 0.7	38.8 ± 0.7	38.7 ± 0.7	38.5 ± 0.7	38.5 ± 0.9	38.5 ± 0.8
	MID	39.1 ± 0.4	39.2 ± 0.5	39.0 ± 0.5	38.8 ± 0.4	38.8 ± 0.6	38.8 ± 0.5
	BUT	39.1 ± 0.6	39.0 ± 0.5	38.9 ± 0.4	38.7 ± 0.3	38.6 ± 0.3	38.6 ± 0.3
	ACEBUT	39.0 ± 0.8	38.9 ± 0.7	38.6 ± 0.4	38.6 ± 0.5	38.4 ± 0.5	38.4 ± 0.5
	MIDBUT	39.0 ± 0.3	39.0 ± 0.4	38.6 ± 0.4	38.5 ± 0.4	38.4 ± 0.5	38.4 ± 0.5

Note: no significant differences ($P < 0.05$) were observed between the 6 groups or between baseline mean and any point within a group.

to access sedation were not large enough to show differences or that the dose of butorphanol administered was not high enough. The sample size, the sedation scoring scale and the dose of butorphanol used in this study are based on those usually reported in similar studies[6,7,14]. The anaesthetic effects of butorphanol in goats have also previously been reported as variable and unpredictable[14]. This unreliability in degree of sedation could be related to butorphanol's behavioural effects associated with central nervous system excitement[6,14]. Butorphanol has been reported to cause restlessness and vocalisation[6]. In the study reported here, we did not notice any excitement in any of the goats when butorphanol was administered for sedation. Instead of accessing degree of sedation only at 20 minutes after premedication as done in this study, the assessment could have been done at many time intervals as sedative effects could have varied with time for the different sedative regimes.

The dose of propofol for induction of general anaesthesia in unpremedicated goats of 5.3 mg/kg observed in this study is similar to doses of 5.1 mg/kg[25] and 5.6 mg/kg[1] reported in the literature. Significant decreases in propofol induction dose requirements were observed in goats that received midazolam alone (39.7 %), midazolam combined with butorphanol (38.1 %) and acepromazine combined with butorphanol (27.8 %). These outcomes largely concur with previous studies which indicated that premedication of goats would decrease the dose of propofol for intubation to 3–4 mg/kg[3,9,16]. At dosages used in this study, premedication regimens incorporating midazolam seemed superior in terms of effect on reduction of propofol induction dose when compared with those incorporating acepromazine. This could be because midazolam has muscle relaxing properties in addition to central nervous system depressing effects or that the dose of midazolam used in this study is relatively more potent than the dose of acepromazine used. The quality of general anesthesia obtained with propofol in goats as assessed by induction score, time to extubation, time to sternal recumbency, time to standing and recovery score did not show any particular premedication regimen to be superior to the control group. This could be due to the fact that goats, by nature, have a good temperament and are not easily excitable[28]. These findings on quality and duration of anaesthesia after propofol induction with or without premedication are similar to findings from other studies in goats[4,9,25,26,27]. Propofol anaesthesia is associated with rapid and smooth recoveries, with extubation time less than 10 minutes and time to standing less than 30 minutes in both premedicated and unpremedicated goats as this study as well as other related studies attest to[4,9,25,26,27]. Occurrence of myoclonic activity (clonic-tonic convulsions and/or opisthotonus) on administration of propofol in a number of species[16], which has been reported in other studies, was observed in a few individual goats in this study. Premedication agents did not seem to influence occurrence of the myoclonic activities as their distribution between groups seemed random.

Table 5: **Respiratory variables** (mean ± standard deviation) **following preanaesthetic administration of saline 1.0 mℓ** (SAL group), **acepromazine 0.05 mg/kg** (ACE group), **midazolam 0.3 mg/kg** (MID group), **butorphanol 0.1 mg/kg** (BUT group), **acepromazine 0.05 mg/kg with butorphanol 0.1 mg/kg** (ACEBUT group), **and midazolam 0.3 mg/kg with butorphanol 0.1 mg/kg** (MIDBUT group) **and then intravenous administration of propofol for induction of general anaesthesia in goats.**

Variable	Group	Baseline	20 minutes post-sedation	Time after induction (minutes)			
				1	10	20	30
Resp. rate (breaths/minute)	SAL	25 ± 4	20 ± 4	13 ± 4	17 ± 3	23 ± 7	23 ± 4
	ACE	22 ± 8	20 ± 9	8 ± 3	17 ± 4	20 ± 5	20 ± 5
	MID	26 ± 7	17 ± 6	12 ± 7*	15 ± 4	19 ± 7	20 ± 4
	BUT	30 ± 6	23 ± 10	18 ± 9	17 ± 5	20 ± 7	20 ± 3
	ACEBUT	29 ± 3	25 ± 9	8 ± 4*	13 ± 6*	17 ± 4	17 ± 6
	MIDBUT	23 ± 7	24 ± 8	10 ± 5	14 ± 3	17 ± 5	19 ± 3
PaO_2 (mmHg)	SAL	85.9 ± 12.8	77.9 ± 9.3			74.8 ± 10.3	
	ACE	79.2 ± 4.4	75.2 ± 9.0			72.1 ± 18.1	
	MID	82.7 ± 3.1	84.6 ± 22.1			71.7 ± 12.6	
	BUT	82.2 ± 7.0	78.6 ± 14.1			87.5 ± 4.6	
	ACEBUT	84.0 ± 6.0	80.3 ± 8.6			98.8 ± 22.1	
	MIDBUT	85.2 ± 8.2	83.3 ± 9.0			77.1 ± 22.2	
$PaCO_2$ (mmHg)	SAL	34.0 ± 1.4	31.9 ± 2.6			34.0 ± 2.6	
	ACE	34.0 ± 2.5	33.5 ± 2.3			36.2 ± 7.5	
	MID	34.6 ± 1.5	32.4 ± 3.0			39.0 ± 8.6	
	BUT	34.3 ± 3.4	33.2 ± 3.7			31.0 ± 6.0	
	ACEBUT	32.8 ± 2.9	32.8 ± 5.2			33.4 ± 4.1	
	MIDBUT	32.3 ± 6.5	31.8 ± 6.7			37.0 ± 7.2	
pHa	SAL	7.46 ± 0.02	7.48 ± 0.03			7.46 ± 0.03	
	ACE	7.43± 0.03	7.44 ± 0.04			7.42 ± 0.03	
	MID	7.45 ± 0.03	7.42 ± 0.03			7.41 ± 0.03	
	BUT	7.47 ± 0.02	7.45 ± 0.04			7.44 ± 0.04	
	ACEBUT	7.45 ± 0.03	7.43 ± 0.04			7.42 ± 0.05	
	MIDBUT	7.46 ± 0.01	7.47 ± 0.02			7.41 ± 0.03	
$[HCO_3^-]$ (mol/litre)	SAL	23.6 ± 1.2	23.0 ± 2.4			23.3 ± 2.6	
	ACE	19.1 ± 8.7	22.3 ± 2.8			22.8 ± 4.0	
	MID	23.7 ± 2.4	20.4 ± 2.8			22.1 ± 1.8	
	BUT	24.7 ± 3.4	23.0 ± 4.5			20.1 ± 5.7	
	ACEBUT	22.3 ± 2.4	21.0 ± 3.4			21.3 ± 3.7	
	MIDBUT	22.4 ± 4.8	22.7 ± 5.8			23.1 ± 3.7	
SaO_2 (%)	SAL	96.8 ± 1.1	96.3 ± 1.0			95.3 ± 1.9	
	ACE	96.1 ± 0.8	95.4 ± 1.7			92.0 ± 9.1	
	MID	96.6 ± 0.4	96.0 ± 1.5			93.6 ± 3.8	
	BUT	96.7 ± 0.7	95.5 ± 3.0			97.0 ± 0.3	
	ACEBUT	96.8 ± 0.4	96.0 ± 1.3			97.1 ± 1.7	
	MIDBUT	96.9 ± 0.4	96.7 ± 0.9			91.9 ± 11.3	

*Significantly different ($P < 0.05$) from baseline reading
PaO_2, arterial oxygen tension; $PaCO_2$, arterial carbon dioxide tension; pHa, arterial hydrogen ion concentration; $[HCO_3^-]$, arterial bicarbonate ion concentration, SaO_2, arterial oxygen saturation.

These myoclonic activities may have been observed as a manifestation of light-plane anaesthesia since all the goats in this study were anaesthetised just deeply enough to allow placement of an endotracheal tube[25]. Some authors disagree with the speculation that higher doses of propofol would ameliorate development of myoclonic activity[26].

The cardiovascular data compared both within and between groups did not show any significant differences and were all within normal physiological ranges. This shows that the premedication regimens used for propofol general anaesthesia at dosages used in this study minimally affected cardiovascular system function. The respiratory system was largely unaffected by the anaesthetic regimens used in this study as indicated by the mean $PaCO_2$ and SaO_2 values obtained, although the respiratory rate decreased considerably soon after administration of propofol for induction of anaesthesia. The fact that propofol is known to cause induction apnoea in most species may explain why respiratory rate decreased soon after its administration to goats in this study[4,17,26]. Arterial blood-gas parameters, which are largely dependent on adequate function of both the respiratory and cardiovascular system in anaesthetised animals[31], were not affected by the type of premedication regimen used in this study and were within normal limits. The findings of the effects of midazolam on arterial blood-gas and acid-base variables are similar to those of another study which showed that midazolam had minimal effects while xylazine caused hypoxaemia and respiratory acidosis in goats[32]. In retrospect, it might have been wise to collect arterial blood gas samples within the first 5 minutes of induction of general anaesthesia, and not after 20 minutes as done in this study, as the depressant effects of propofol on the respiratory system might have been more pronounced at this early time.

It is concluded that sedation of goats with midazolam alone, and combinations of butorphanol with acepromazine or midazolam, reduces the dose of propofol required for induction of general anaesthesia in goats, with minimal effects on cardiopulmonary function.

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