CARDIOPULMONARY AND STRESS RESPONSES OF XYLAZINE, ACEPROMAZINE OR MIDAZOLAM SEDATED WEST AFRICAN DWARF GOATS TO DIFFERENT BODY POSITIONING

BY

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CERTIFICATION

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DEDICATION

This work is dedicated to Almighty God, for granting me the grace to start and finish this work. I am nothing without my creator, I return all the glory to you Lord.

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ABSTRACT

West African Dwarf (WAD) goats serve as an important source of animal protein, are ubiquitous in rural Nigerian households and often undergo surgical procedures. Induction of general anaesthesia in goats is associated with resultant severe systemic side effects depending on the drug and due to position-induced stress. Information on the responses of sedated WAD goats to different sedatives and varying body positioning is not yet reported. Therefore, the study was designed to investigate cardiopulmonary and stress responses of WAD goats to xylazine, acepromazine or midazolam sedation in different body positioning.

Adult WAD bucks (n=6), mean body weight of 11±2.0 kg were randomly selected for three separate experiments using xylazine, acepromazine or midazolam in five clinical trials lasting five days each. Sedation was achieved by intramuscular administration of xylazine (0.05mg/kg), acepromazine (0.2 mg/kg) or midazolam (0.3 mg/kg). For each experiment, goats were restrained in standing (control), Right Lateral (RL), Left Lateral (LL), supine and prone positions. Venous blood (5 ml) via jugular venipuncture was collected before and after each trial to determine selected stress biomarkers [blood glucose (mg/dL), plasma cortisol (mmol/L) and lactate dehydrogenase LDH (U/L)] using specific kits and Autoanalyser®. Heart Rate -HR (beats/minute), Respiratory Rate -RR (breaths/minute), Mean Arterial Pressure -MAP (mmHg), Oxygen-haemoglobin Saturation -SpO_2 (%) and Rectal Temperature -RT (°C) were measured at intervals of 10 minutes for one hour using multiparameter monitor®. The bucks were rested for 14 days in between clinical trials. Data were analysed using descriptive statistics and ANOVA at $\alpha_{0.05.}$

In LL, supine and prone body positions, peak blood glucose levels and plasma cortisol, respectively were significantly increased with xylazine (210.8±55.5; 44.0±32.3), acepromazine (121.0±70.4; 137.5±80.2) and midazolam (90.5±40.8; 97.3±31.5) compared to control (78.5±15.4; 14.7±9.1). Plasma levels of LDH (213.7±36.7 to 358.2±96.6) were significantly decreased compared to control (282.3±48.5 to 706.2±711.9) for the RL, LL, supine and prone positions with xylazine and acepromazine sedation. Significant decreases in HR (59.5±8.2 to 65.0±5.8) were observed with xylazine in all the body positions except in prone compared to control (72.4±23.4 to 78.6±31.4), while acepromazine and midazolam had highest HR with supine position. Xylazine sedation increased RR for the LL (37.2±18.9) versus control (30.3±13.9). Acepromazine and midazolam did not show any significant changes in RR for all body positions. Xylazine and acepromazine sedation resulted in significant decrease in MAP for the RL (45.3±19.5 to 70.0±10.5), LL (50.7±5.8 to 64.2±17.8) and supine (42.0±10.6 to 62.5±22.3) positions compared to control (61.3±10.1 to 87.0±10.7). However, midazolam sedation did not show significant changes in MAP in other body positions. No significant decrease was observed for SpO_2 and RT with any of the sedatives regardless of body positions.

Xylazine sedation resulted in severe hypotension and hyperglycaemia with left lateral and supine body positions whereas acepromazine and midazolam sedation resulted in mild hypotension and increased heart rate with the left lateral and prone body positions. The left lateral and prone positioning should therefore be avoided in caprine sedation. Acepromazine and midazolam are considered safer alternatives to xylazine for sedation in West African Dwarf goats.

Keywords: Body positioning, Cardiopulmonary stress responses, Sedation, West African Dwarf goats

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LIST OF ABBREVIATIONS

HR	Heart rate
LDH	Lactate Dehydration
LL	Left Lateral position
MAP	Mean Arterial Pressure
PP	Prone position
RL	Right Lateral position
RR	Respiratory rate
RT	Rectal temperature
SPO2	Oxygen haemoglobin saturation
STP	Standing Position
SUP	Supine position
WAD	West African Dwarf

CHAPTER ONE

INTRODUCTION

1.1 Background to the Study

The estimated population of goats in Nigeria is put at about 34.5million (RIM, 1992) of which West African Dwarf (WAD) breed are the commonest (about 45%) of this population.They are reared for different reasons at different locations (Ajala *et al*., 2008; Olatunji-Akioye & Adeyemo, 2019). Goats are very important to the increasing population as source of animal protein and regular income especially for the rural populace (Chiejina *et al*., 2015; Fasae *et al.,* 2015). Their compatibility with rural communities is exemplified by their ability to graze and utilize poor quality forage, walk long distances, short generation interval, high reproductive rate, and low risk on investments (Lebbie, 2004).An ever increasing population in Nigeria places a greater demand on goat supply and this also leads to a steady rise in the population of goats reared in the country (Okpeku *et al*., 2011). Thecommon management system practice of rearing goats in Nigeria is semi-intensive, this method exposes them to various harsh weather condition and health challenges including rumen foreign body impaction, laceration from sharp twigs and grasses, which consequently necessitate handling, medical, diagnostic or surgical intervention (Abu *et al*., 2013).

Most of several unique complications from sedation and anaesthesia in ruminants arise from the interaction of alimentary and respiration systems (Adetunji *et al*., 1985; Clarke *et al*., 2014).Loss of eructation usually accompanies sedation and general anaesthesia with continued fermentation. In the absence of eructation, gas accumulation in the rumen relates directly to the rate of gas produced from fermentation. Gas distension of the rumen may depress respiratory function by reducing the lung volume and venous return (Musewe *et al*., 1979; Valverde and Doherty, 2008). Regurgitation of ruminal content is common after light/active regurgitation, vomiting and deep (passive or silent regurgitation) general anaesthesia. Active regurgitation follows complicated and coordinated series of unsuppressed reflex

mechanisms in order to remove unwanted materials from the digestive tract whereas passive regurgitation results from relaxed oesophageal musculature and transruminal pressure gradients (Thurmon and Benson, 1981; Thurmon and Benson, 1993).

Also, large volume of saliva is secreted to maintain fluid volume and steady state condition of pH and ionic ruminal composition. This saliva secretion continues even during general anaesthesia, which is of great physiologic consideration as this may cause airway blockage or aspiration (Galatos, 2011). Both regurgitated material and saliva have potential for aspiration into the lungs of the animal whose airway is unprotected (Steffey, 1986). The solid component of aspirated material can block the airway, the liquid component can flood the alveoli and finally the microbial component can cause localized or generalized sepsis with fatal consequences.

A proper body position ideally should provide an unrestricted access to the operative site, should not interfere with peripheral tissue perfusion, ventilation, and oxygenation and should not put undue pressure on neuromuscular system and joints, otherwise this is stressful for the animal.In the goat, various surgical procedures have been done with right-lateral position, including surgeries of forestomach (rumenotomy and rumenostomy), oesophagus (oesophagotomy) and gravid uterus(Caesarean section) while the left-lateral position is indicated for the procedures on the abomasum and intestine (Fabini and Ducharme 2014).The supine position is indicated in the goats for procedures on the udder, umbilicus, urinary bladder, abomasal displacement and genital organs such as preparation of teaser buck while prone position is indicated for cerebrospinal fluid (CSF) tap, myelography and spinal procedures (Fabini and Ducharme 2014). Reports have shown that a number of variables, including handling and animal behaviour can elicit stress in animals (Hemsworth *et al*., 2011).

Stress is an adaptive event of neuroendocrine, metabolic, haematological, immune and behavioural changes following anxiety, pain, trauma or injury designed towards the restoration or maintenance of homeostasis (Desborough, 2000; Allen *et al*., 2014). A stressor is capable of disrupting homeostasis as it is normally accompanied by series of predictable events such as biochemical, physiological, cognitive and behavioural changes (Taylor, 2008). The neuroendocrine response to stress includes elevated circulating catecholamines and cortisol (Finnerty *et al*., 2013; Saidu *et al*., 2016).Behavioural changes in response to stress in animals include flight and fight,

immobility (freezing stance), panting, sweating, piloerection and facial expression (Breazile, 1987). Hyperglycaemia has also been reported as one of the markers of stress via the activation of various glucose pathways (Armario *et al*., 1995).

1.2 Statement of the Problem

Naturally, all ruminants voluntarily assume either the standing or sternal position when ruminating,resting or sleeping.Any other body positions would appear to be unphysiological.Indeed, awake or sedated cattle placed in either lateral or supine position showed significant cardiopulmonary disturbances and intense stress(Adetunji *et al.,* 1984; Wagner *et al.*, 1990; Tagawa *et al*., 1994).They are generally not used to handling, thus when presented for clinical procedures, there is the need for physical restraint, sedation, or anaesthesia,which in turn initiates stress response especially in long term recumbency.Also, they are considered poor subjects for general anaesthesia because of the associated complications such as inadequate ventilation, prolonged recumbency, ruminal tympany, regurgitation and excessive salivation with potential for aspiration into the lungs (Adetunji *et al.,* 1984; Clarke *et al*., 2014). Consequently, sedation and loco-regional anaesthesia are usually employed in ruminants for clinical procedures.

Most clinical procedures in large ruminants such as cattle are performed on the standing animal with the aid of sedation under loco-regional analgesia and/or restraining chute (Fabini and Ducharme, 2004).However, standing procedures are not practical for small ruminants such as goat and sheep owing to their small body size and they have to be made recumbent for this purpose (Clarke *et al*., 2014). Considering that goats differ considerably from cattle with regard to species, body size and body weight, it would seem inappropriate to extrapolate large ruminant data to the goat as a basis for providing supportive care.

Body positionsmost used in the goatsare Right-Lateral (RL), Left-Lateral (LL),Supine (SUP) and Prone (PP) positions(Fabini and Ducharme, 2004; Ames, 2014). Physiological effects of these positions are yet to be reported in sedated sheep and goat. Therefore, the responses of sedated goat or sheep to different body positions are not known at the present time.

1.3 Research Question

What are the cardiopulmonary and stress responses of sedated WAD goats to different body positioning?

1.4 Null Hypothesis

There are no differences in cardiopulmonary and stress responses of sedated goats to different body positions.

1.5 Aim of the Research

The aim of this research was to determine and compare cardiopulmonary and stress responses of sedated goats placed in different body positions.

1.6 Objectives of Research

To compare the cardiopulmonary responses of xylazine-sedated goats to standing, right-lateral, left lateral, supine and prone positions.

To compare the stress responses of xylazine-sedated goats to standing, right-lateral, left lateral, supine and prone positions.

To compare the cardiopulmonary responses of acepromazine-sedated goats to standing right-lateral, left-lateral, supine and prone body positions.

To compare the stress responses of acepromazine-sedated goats to standing right-lateral, left-lateral, supine and prone body positions.

To compare the cardiopulmonary responses of midazolam-sedated goats to standing, right-lateral, left-lateral supine and prone body positions.

To compare the stress responses of midazolam-sedated goats to standing, right-lateral, left-lateral supine and prone body positions.

1.7 Justification for the Research

In most developing countries like Nigeria, policy makers and planners tend to focus on small ruminants production as a part of solution to the current problem of food insecurity. Since optimal animal production depends partly on animal health maintenance, research efforts at improving or maintaining goat health are clearly

desirable. Therefore, goats are frequently presented for diagnostic, medical and surgical procedures (Fabini and Ducharme 2004).

The choice of appropriate and safe body positioning should facilitate the conduct of the intended diagnostic, medical and surgical procedures and also promote recuperation of the ruminant patient in the perioperative period and intensive care unit.

The ultimate cellular need is an adequate oxygen delivery to the tissue and the removal of metabolic waste. The uptake, delivery, extraction and use of oxygen by the metabolising tissues depend on the integrated functions of multiple organ systems, including lung function, cardiac pump function, blood-oxygen carrying capacity, blood viscosity, vascular tone, global and regional distribution of blood flow and tissue metabolism. Indeed, a distinct separation of the gas transport role of respiration and circulation is not possible (Schumaker and Cain, 1987). Thus, constant monitoring of both life support systems should enable the clinician to make rational decisions regarding the required interventions.

Although, physiological stress produces beneficial effects, excessive stress (distress) causes unwanted haemodynamic changes, restrict glucose available for tissues utilization, depress immune system function and elongate wound healing or tissue repair (Muir, 1990; Finnerty *et al*., 2013). Therefore, factual information obtained from this research should be of particular interest to all goat veterinary caregivers, such as the surgeons, anaesthetists, internists and nurses including the physiologists and research scientists that use the goat as an experimental model.

CHAPTER TWO

2.0 LITERATURE REVIEW

In veterinary practice, goats are often presented for diagnostic, medical and surgical procedures necessitating sedation, anaesthesia, restrain and body positioning. The commonly used classes of sedatives in caprine practice include alpha$_2$-agonists (e.g. xylazine, medetomidine, detomidine and dexmedetomidine), phenothiazine derivative (e.g. acepromazine) and benzodiazepines e.g. diazepam, midazolam and zolazepam (Taylor 1991, Udegbunam and Adetunji 2007). The body positions used in goats are right-lateral, left-lateral, supine and prone positions. In this review, WAD goats,anaesthesia, pharmacology of commonly used sedatives, body positioning, cardiopulmonary physiology and biological response to stress will be considered with reference to small ruminants.

2.1 West African Dwarf Goats

The earliest domesticated animal (ruminant) after wolf is the goat (Zeder and Hasse, 2000). Goats are highly prolific among ruminants as they are resourceful and efficient in producing milk, meat, leather or skin (Morand-Fehr, 2004; Lebbie, 2004). West African Dwarf goats are the most abundant small ruminant in Nigeria, about 85% of them reportedly kept by peasant and uneducated farmers, villagers and owners of small business(Chiejina*et al*., 2015; FAOSTAT, 2011). Their dominance in the rural region is as a result of their ability to graze and utilize poor quality forage,roam long distances, short generation interval, high fertility rate and low risk on investments (Lebbie, 2004). They are as such important financial assets, as consumption and sales of their products provide financial support forfamilies in times of draught and inflation (Lebbie, 2004). West African Dwarf (WAD) goat is one of the major animal protein sources for the ever increasing population in Nigeria, this is because it is cheap and thus affordable (Gambo *et al.*, 2004). Aside this, it has been reported that micro livestock farming can improve economic turnover of an individual and consequently improve the standard of living of the populace (Okpeku *et al*., 2011).

2.2 Anaesthesia in Ruminants

In veterinary medicine and surgery practice, anaesthesia plays essential roles during performance of diagnostic or minor surgical procedures in small ruminants (Galatos, 2011). It produces analgesia and unconsciousness during painful procedures, used as chemical restraints and/or immobility of apprehensive animal patients and produces skeletal muscle relaxation during required procedures (Galatos, 2011). Commonly administered injectable general anaesthetics in practice arealfaxalone, propofol, ketamine, barbiturates, and etomidate (Clarke *et al,* 2014). However, general anaesthesia is associated with many undesirable effects in ruminantssuch as secretion of large volumes of saliva, which continues during anesthesia and may cause airway obstruction or aspiration into the lungs (Adetunji *et al.,* 1984; Clarke *et al*., 2014). Also, pneumonia or asphyxiation can occur during deep anaesthesia or when endotracheal intubation is attempted in light anaesthesia especiallywhen the animal is in dorsal or lateral recumbency (Valverde and Doherty, 2008).Consequently, the use of general anaesthesia impairs eructation, continuous fermentation of ingesta, which accumulate in the rumen and cause bloat and respiratory distress (Valverde and Doherty, 2008). Moreover, most general anaesthetics licensed for use in small ruminants are expensive and limited in number, thus these may influence the use of general anaesthesia due to economic consideration (Galatos, 2011; Fasae*et al.,* 2015).

2.2.1 Sedation in Ruminants

The use of sedatives in ruminants make handling and induction of anxious animals safer, reduces the anaesthetic dose requirement, provision of pre-emptive analgesia, counteract the side effect of other drugs and facilitate smooth recovery (Riebold, 2007). In most cases, sedation is used with loco-regional anaesthesia in ruminants to perform various procedures to avoid several aftereffectsrelated with the use of general anaesthesia (Fabini and Ducharme, 2004; Valverde and Doherty, 2008).In addition, use of sedative and loco-regional anaesthesia requires minimal equipment, low cost, and minimal cardiopulmonary depression (Hall *et al*., 2001;Skarda and Tranquilli, 2007). Commonly used sedatives in ruminants are xylazine, acepromazine, diazepam and midazolam (Kastner, 2006; Valverde and Doherty, 2008).

2.3 Pharmacology of Alpha$_2$Agonists

2.3.1 Xylazine

Initially, xylazine was produced in 1962 by Bayer (Leverkusen, Germany) for the treatment of hypertension. It has become popular in the Europe as alpha-2-agonist as analgesics, sedatives and anaesthetic adjunct in animals (Kerr *et al*., 1972). It is the most popularly used alpha$_2$ agonist; romifidine, dexmedetomidine and detomidine are less used (Kastner, 2006).

Xylazine being an alpha adrenoceptor agonist produces potent sedation, deep analgesia and satisfactory muscle relaxation in ruminants. In clinical practice, xylazine is employed as chemical restraint or anaesthetic adjunct in ruminants (Udegbunam and Adetunji, 2007; Huichu, 2014).

2.3.2 Mechanism of Action

Xylazine activates alpha adrenoceptors directly in different tissues. It induces sedation by activating central α_2-receptors (Hsu 1981), which modulate the release of norepinephrine thatis necessary for arousal (Kobinger, 1978; Skarda and Muir, 1992). Through a central mechanism, xylazine enhancesactivity mediated bybaroreceptor and vagus nerve (Antonaccio *et al*., 1973). Also, xylazine induces analgesia and muscle relaxation when administered to cattle (Kastner, 2006; Huichu, 2014) by impeding intraneuronal transmission of impulses (Booth, 1982). Currently, several alpha$_2$ adrenoceptor subtypes that have been identified are alpha$_{2A}$, alpha$_{2B,}$ alpha$_{2c,}$ and alpha2$_D$ (Regan and Cotecchia, 1992).In different species, subtypes vary in distribution and receptor densities (Alex, 2010). Alpha$_{2A}$, alpha$_{2B}$ and alpha$_{2C}$receptors are thought to produce analgesic actions seen in the use of alpha$_2$ agonist drugs while alpha$_{2D}$ subtype is predominant in the sheep brain and this explains the sensitivity of ruminants to alpha$_2$ agonists thus requiring lower doses to cause sedative effects when compared to other species (Riviere and Papich, 2009).

2.3.3 Sedatives Effect

The blockade of norepinephrine release after administration of xylazine results in sedation. Since pre-existing stress, pain and excitement increase endogenous catecholamine release, full sedation may not be achieved under these conditions (Saleh, 1993). Behaviourally, all alpha$_2$ agonists produce similar effects in goats including initial nervousness, head lowering, nictating membraneand tonguebulging, partial drooling of eyelids and ataxia (Skarda and Muir, 1992). In addition, there is reduced awareness to the surrounding although the animal maybe stimulated by sudden touch or surrounding noise. In all alpha$_2$ agonists, the onset of sedation is usually slower with intramuscular than intravenous injection (Clarke *et al*., 2014). Ruminants have profound sensitivity to sedative effects of alpha$_2$ agonists. It has been reported that goats given 0.1mg/kg intramuscular injection of xylazine produced maximal effect in five minute and lasted over an hour (Shah *et al*., 2013). Sedation with xylazine depends on the dose and temperament of the animal (Valverde and Doherty, 2008). Increased sedation time has been reported to accompany incremental dose, whereas depth of sedation was not altered (Dugdale, 2010).

2.3.4 Analgesic Effect

Alpha$_2$ agonists produce analgesic effect through activation of receptors within the central nervous system wheresignals are usually initiatedthrough modulations of nociceptive stimulus(Sternberg, 1989). Studies have also suggestedthat alpha$_2$ agonists produce antinociceptive effect via presynaptic and postsynaptic inhibitory effects (Yaksh, 1985).

The interactivity between alpha$_2$ adrenoceptors and hypnotic receptors situatedwithin the central nervous system also result in modulation of pain (Osmote *et al*., 1991). There is clinical evidence that analgesia does not last as long as sedation and also that the agent alone cannot be used for major painful or surgical procedure (Shah*et al*., 2013). Breed and/or mass of the ruminant have been observed to influence the analgesic effect of xylazine (Ley *et al*., 1991).

2.3.5 Cardiopulmonary Effect

All alpha$_2$ agonists cause bradycardia and related bradyarrythmia, as well asmarkedincreasein systemic vascular resistance (Pypendop and Verstegen, 1998). The

induced bradycardia may result from several mechanisms in addition to reductionin central sympathetic outflow, direct pacemakerand conducting fibersdepression, inhibited norepinephrine release and an elevated acetylcholine release from autonomic nerves (Paddleford and Harvey, 1999). The consequent decreased cardiac output is as a result of initialresponse of baroreceptor and central sympatholytic action resulting in a slowing heart rate. Activation of alpha$_2$ receptors within vascular smooth muscles result in vasoconstriction with increased systemic vascular resistance (Lammintausta, 1991).

Intravenous administration of xylazine causes initial transient hypertension followed by hypotension (Hsu *et al*., 1985). The xylazine-induced hypertension was linked with direct activation of alpha receptor in peripheral vessels whereas the induced hypotension was due to depression of central sympathetic output (Merin, 1986). In calves, cardiac output decreased for 0 minutes following xylazine administration. The effect of these cardiovascular alterations depends on dose rate of alpha$_2$ agonist administered, health status of the patient and concurrent administration with other drugs. In ruminants,xylazine may produce cardiopulmonary depression and temporary hyperglycaemia (Derossi *et al*., 2003).

In sheep, injection of xylazine results in constriction of bronchus, increased pulmonary vascular resistanceand pulmonary oedema with or without hypoxaemia (Kastner *et al*., 2006; Raisis*et al*., 2021). In general, alpha$_2$ agonists tend to cause gut stasis resulting in bloat, which further impair ventilation (Uggla and Zindquist, 1983). Transient apnoea, tachypnoea and deep breathing have been reported in goats. In addition, concurrent tidal volume decreased in sheep and goats (Mohammed *et al*., 1996).

2.3.6 Dosage

In cattle, xylazine is given at dose rate of 0.1mg per kg IV or 0.2mg per kg IM (Trim, 1987), sedation in goats requires 0.05 to 0.1mg per kg intramuscular injection (Clarke *et al*., 2014).

2.4 Pharmacology of Acepromazine

This is a phenothiazine derivative that is commonly used in veterinary medicine. It produces mild tranquilization in various animal species (Lemke, 2007). Clinically, relevant doses can be used solely as sedatives or as adjunct for premedication prior to anaesthesia (Dohertyet *al*., 2002). Beside the sedative and calming effects, acepromazine produces antiarrhythmic and antiemetic effects (Taylor, 1991).

2.4.1 Mechanism of Action

Acepromazine produces calming neurologic effect by depressing the reticular activating system (RAS) and by obstructing dopaminergic receptors in the CNS (Ebert *et al*., 2002). It also suppresses the sympathetic nervous system leading to a reduction in catecholamine release centrally and peripherally. Acepromazine may lower seizure threshold in animals but it inhibits ketamine-induced seizures (McConnell *et al*., 2007). It produces antiemetic action through blocking of dopamine interaction with Chemoreceptor Trigger Zone (CTZ) in the medulla. It also has potential to produce relaxation of oesophagus and cardia consequently predisposingruminants toregurgitation (Taylor, 1991).

2.4.2. Cardiopulmonary Effect

Blockade of alpha-adrenergic receptor causes vasodilation with subsequent decrease in blood pressure (Alvaides *et al*., 2008). Excited or apprehensive animals are more prone to developing hypotension. With calmness, heart rate decreases but reflex tachycardia may occur as hypotension develops. Thus, when heart rate increases during the use of acepromazine, it is to compensate for the decreased systemic vascular resistance and blood pressure (Muir *et al*., 1979; Pequito *et al*., 2012). Also, acepromazine depresses the thermoregulatory center, predisposing to decrease in body temperature (Valverde and Doherty, 2008; Huichu, 2014). It often decreases respiratory rate but increases the tidal volume to maintain adequate minute ventilation (Muir *et al*., 1979). Thus, the effect of acepromazine of the pulmonary function is minimal.

2.4.3 Sedative Effect

Acepromazine produces mental calming, reduce mental activity and raises threshold for responding to external stimuli. Although, not an analgesic, it improves the

analgesic action of other drugs. An adequate stimulus can temporarily reverse the calming effect. At recommended doses, the sedative effect of acepromazine lasts for 2-4 hours, although it may last up to 4-8hours (Thurmon and Benson, 1993).

2.4.4 Dosage

In small ruminants, acepromazine is administered at a dose rate of 0.05-0.1mg per kg intramuscularly for mild tranquilization and minimal cardiopulmonary function (Dzikiti *et al*., 2009). In sheep and goats, doses from 0.1-0.3mg/kg scan be injected intravenously (IV) or IM to produce transquilization (Lin *et al*., 2012). Over dosage with acepromazine can cause involuntary musculoskeletal effects in animals (Clarke *et al*., 2014).

2.5 Pharmacology of Midazolam

It belongs to benzodiazepine class of sedative, water-soluble agent commonly administered in veterinary medicine for its anticonvulsant, anxiolytic and muscle relaxant activities (Cao *et al*., 2002). Unlike other benzodiazepines, it does not cause tissue irritation as it is rapidly absorbed and easy to administer intravenously or intramuscularly incooperative animals (Valverde and Doherty, 2008).

2.5.1 Mechanism of Action

Midazolam, due to its high water-soluble property is able to cross the blood-brain barrier rapidly to producecentral muscle relaxant effect. It produces its effect by potentiatinginhibition of neurone,which is mediated by Gamma Amino Butyric Acid (GABA) (Mohler *et al.,*2002; Lemke, 2007; Olkkola and Ahohen, 2008).

2.5.2 Cardiopulmonary Effect

The cardiovascular effects of midazolam are mild in most instances thus it can be used in high-risk animal patients such as geriatric or debilitated animals (Lemke, 2007; Dzikiti *et al*.,2014). It has a central effect on the vasomotor centres thus reducing arterial pressure and elevating heart rate due to decrease in systemic vascular resistance (Katzung, 2004). Midazolam has been shown to induce a mild reduction in cardiac output and depress baroreflex thus restricting ability to compensate for haemodynamic changes associated with hypovolaemia (Marty *et al*., 1986). Essentially, midazolam does not have profound effect on the respiratory system.

2.5.3 Sedative Effect

Midazolam is frequently administered to reduce the central excitatory effect of ketamine. It is also co-administered during anaesthetic induction to reduce the dose of other injectable anaesthetics (Sanches *et al*.,2013). It is metabolized in the microsomal enzymes of the liver and its effects after administration have been shown to be dose-dependent in goats (Benson and Thurmon, 1979).

2.5.4 Dosage

In goats, midazolam administration is at 0.3-0.6mg per kg IM to achieve hypnosis and light sedation (Kyle *et al.,* 1995; Clarke *et al*., 2014). Sheep responding to mechanical pain have shown decrease in response to pain after being administered 0.2mg/kg and midazolam (Kyle *et al.,* 1995).

2.6 Applied ruminant anatomy

This section reviews aspect of ruminant anatomy that is relevant to clinical management of the animals. This includes size and body weight, alimentary tract, cardiopulmonary systems and neuromuscular system. Body weight of small ruminants range between 1kg to 40kg. On the other hand, cattle may reach up to 1000kg. The size of the animal determines the choice of anaesthetic equipment such as endotracheal tube and anaesthetic circuit. Also, the ease of animal handling is determined by the size. The diversity of size in this ruminant group requires large equipment inventory (Steffey, 1986). The unique and large size of ruminant stomach may sometimes force the diaphragm cranially and thus reduce the volume of the lung. Ruminant stomach occupies about three quarters of the abdominal cavity and is closely related to the diaphragm. The stomach consists of 80% rumen, 5% reticulum, 7% omasum and 8% abomasum. In sheep and goats, the stomach capacity is about 15-18L (Getty, 1975). Saliva is secreted in large volume in ruminants to maintain the fluid volume and steady pH and ionic composition of the rumen. Total volume of saliva in small ruminants has been reported to be 6-16L per 24 hours (Kay, 1960). Anaesthesia may depress the function of the stomach by influencing the factors that impact on the cardiopulmonary function (West, 1970; Musewe *et al*., 1979).

Endotracheal intubation in ruminants can be very difficult and nearly impossible because they have jaws that do not open widely, long narrow oral cavity and laryngeal openings (Steffey, 1986). In domestic animals, the lungs are divided into lobes, inspired air is supplied to these lobes through the trachea, which branches into bronchi. However, ruminants have right cranial lobe bronchus, which arises directly from the trachea at about the level of the third rib instead of the mainstem bronchus (Getty, 1975).

General clinical impression is that improper body positioning and prolonged recumbency may lead to postanaesthetic neuropathy or myopathy. Furthermore, incidence and severity of pathology increases directly with the animal patient size thus big animals are more at risk than the small animals. Cellular necrosis and reduced blood flow are consequences of prolonged tissue compression secondary to recumbency and overlying skeletal and muscle mass. External compression of major vessels or drug-induced reduction of cardiac output may also diminish local blood flow (Cox *et al*., 1982).

2.7 Body positioning

In a study carried out on healthy awake cattle (Musewe, 1978) to determine the nature and magnitude of the effect of recumbency on respiratory system mechanics, there was a rise in intraluminal and intraperitoneal pressure and the diaphragm was forced further into the thoracic cavity by the higher peritoneal pressure. Furthermore, it was reported that there was an increase in respiratory resistance and altered respiratory pattern due to changes in the contractile activity of the inspiratory muscles to reduce the work of breathing. In another study by Adetunji and others (1985), evaluating the cardiopulmonary effects of different chemical restraining agents in supine cows, it was reported that supine position produced respiratory embarrassment. It has been reported by Wagner and others that in cattle positioned in lateral recumbency, the weight of the abdominal visceral shifted cranially, thus pushing the diaphragm towards thoracic cavity and diminishing functional residual capacity of the lungs.Consequently, increase in ventilation-perfusion mismatch might result in significant hypoventilation and hypoxaemia (Tagawa *et al*., 1995; Huichu, 2014).To date, such report is not available for goats.

2.7.1 Right-Lateral body position

In this position, with the head over flexed, the airway is prone to partial obstruction. In a study involving awake cattle restrained in right-lateral position, heart rate and mean arterial pressure did not change significantly after 30min (Tagawa *et al*., 1994). In goats anaesthetized with intravenously administered xylazine-ketamine and placed in right-lateral position, within 20 minutes, heart rate and rectal temperature decreased significantly while respiratory rate remained unchanged (Udegbunam & Adetunji, 2005).

2.7.2 Left-Lateral body position

In goats, the left-lateral position is indicated for the procedures on the abomasum and intestine (Fabini & Ducharme, 2014). Cardiopulmonary effect of the left-lateral body position is yet to be reported.

2.7.3 Supine position

In cattle restrained in the supine position for the surgical correction of abomasal displacement, it was reported that the cardiopulmonary parameters and temperature were significantly increased above baseline value (Klein and Fisher, 1998). Also, Adetunji and others in 1985 reported that xylazine-sedated supine cows had significantly lower cardiac index, hypotension and tachycardia than did laterally recumbent cows. Furthermore, acepromazine-sedated supine cows had mean cardiac index, pulmonary arterial pressure and arterial oxygen tension significantly decreased than the corresponding values. In anaesthetized goat, Udegbunam and Adetunji in 2005 reported that mean cardiopulmonary parameters and temperature significantly decreased from the baseline values.

2.7.4 Prone body position

Cardiopulmonary effects of the prone position have not been reported either in cattle or small ruminants.

2.8 Cardiopulmonary Monitoring

Continual monitoring of sedated or anaesthetised small ruminants is important to avoid complications (Lin and Pugh, 2002). Monitoring equipment facilitates easy assessment

and prompt intervention in case of emergency, absence of this makes it difficult to assess depth of sedation or anaesthesia in small ruminants (Riebold, 2007). Major significance of the cardiopulmonary system is deliveryof oxygen to tissues and removal of carbon dioxidesreleased during metabolism. To achieve these functions, the respiratory and cardiovascular systems must work in close concert. The concept of oxygen pathway is clinically useful as itprovides a logical framework for assessment and correction of cardiopulmonary disturbances. The uptake, delivery, extraction and use of oxygen by the metabolizing tissues depend on the integrated functions of multiple organ systems, including lung function, cardiac pump function, blood viscosity, vascular tone, global and regional distribution of blood flow and tissue metabolism (Muir & Welman, 2003) (Figure 3.1).

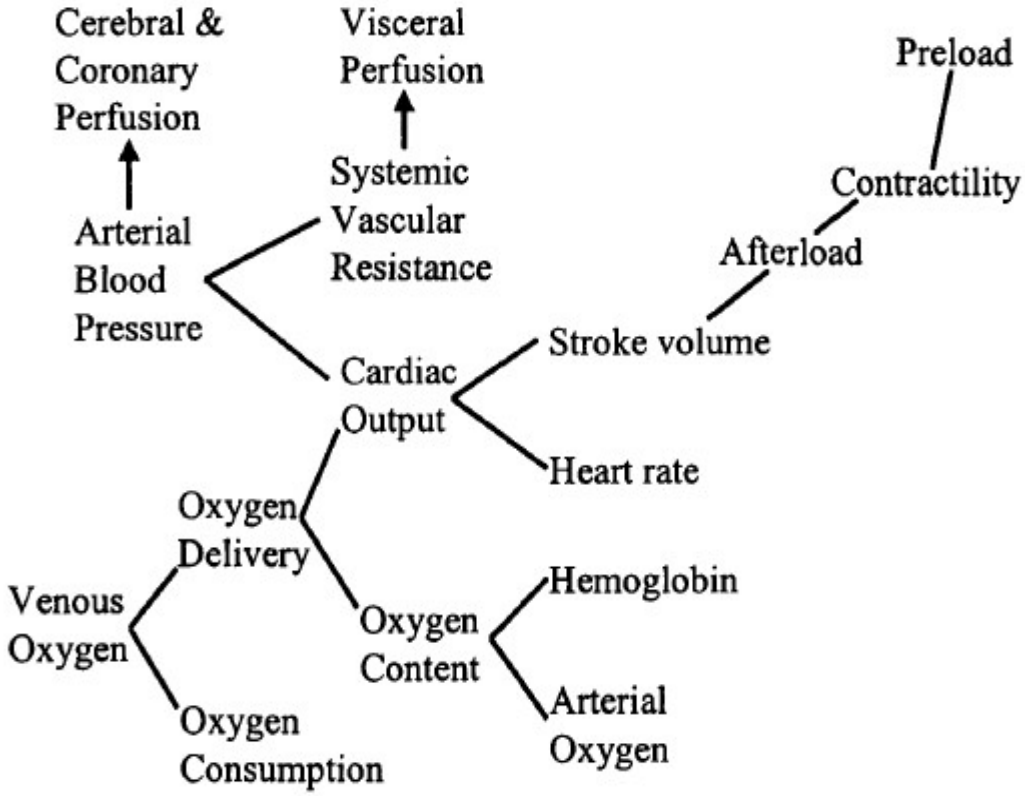

Figure 2.1: Integrated Function of Cardiovascular and Pulmonary systems

(Muir and Welman, 2003)

2.8.1 Ventilation

This can be defined as interchange of the air to and fro of the lungs. It depends on adequate function of the neuromuscular apparatus that supports breathing, coupling of thoracic wall and diaphragm to the lungs and tolerable limits on the work of breathing. Thus, ventilation can be impaired by the neuromuscular injury or depression conditions within the pleural space, or increases in the work of breathing due to pulmonary disease (Steffey and Robinson,1983).

Poor ventilatory effort may occur immediately after operative procedure, when the influence of anaesthetic drug is still present (Riebold, 2007). Therefore,clinical assessment of ventilationstarts with the observation of breathing. Information can be derived from observations of the trend of rebreathing. Animals that are not thermoregulating adopt a pattern of breathing which reduces respiratory work. Normal breathing balances the work necessary to overcome lung compliance (elastic force) and airway resistance (viscous forces) by varying the depth and rate of breathing (Steffey and Robinson, 1983). Animals with restrictive lung conditions such as pulmonary oedema and pneumothorax adjust to a fast and shallow breathing pattern but animals with obstructive lung condition are able to adopt slow and forced breathing pattern (West, 2005).

Ventilometry and Dead space

Ventilation is likely inadequate in animals with low tidal and minutes volume. However, because the distribution of total ventilation between dead space ventilation and alveolar ventilation varies, measurement of normal total ventilation does not ensure that alveolar ventilation is adequate. For this reason, assessment of the adequacy ventilation is based on measurement of partial pressure of carbon dioxide (West, 2005). During ventilation, not all gases reach the area of gas exchange. Consequently, total ventilation is divided between alveolar ventilation and dead space ventilation. Anatomical dead space ventilation flow to areas not involved in gas exchange (Steffey and Robinson, 1983).

2.8.2 Pulmonary Gas Exchange

Gas exchange can be defined as the exchangegases between alveoli and pulmonary venous blood. Ideally, PaO_2should be almost equal to the oxygen gas diffused in

thealveoli, which in turn, is determined by alveolar ventilation (West, 2015). Hypoxaemia can be caused by low inspired oxygen concentration, hypoventilation or venous admixture. Also, hypoxaemia can be due to reduced venous oxygen content (Bishop *et al*., 1988). Hypoventilation is defined byan increased $PaCO_2$or one of its surrogate markers: end-tidal carbondioxide or central venous $PaCO_{2..}$ A $PaCO_2$higher than 60mmHg in small animals may be associated with excessive respiratory acidosis considered to represent suffificient hypoventilation.Increment of inspired oxygen concentration is a potent method of preventing and treatment of hypoxaemia caused by hypoventilation. (Haskin, 2005).

Ventilation-Perfusion Mismatch (V/Q)

Venous admixture can be resulted from low ventilation-perfusion ratio (V/Q), micro or stenotic airway and alveolar collapse, diffusion defect and anatomic right-to-left shunts. Common mechanism of low V/Q hypoxaemia is very responsive to oxygen therapy like global hypoventilation. Instances when ruminants are positioned in dorsal or lateral recumbency or gravid uterus results in pulmonary ventilation-perfusion mismatch, this is due to compression of major abdominal vessels, which impede on venous return thus reducing cardiac output, tissue perfusion and arterial pressure (Thurmon and Benson, 1993).

Oxygen delivery

The delivery of oxygen to issues depends on cardiac output,arterial blood oxygen concentration, functional density with characteristic of blood flow (Schumaker and Cain, 1987). Infiltration of oxygen to tissues and the capacity for oxygen delivery suffer if either the ability of the heart to eject blood (cardiac output) is affected or oxygen carrying capacity of the blood is reduced. Monitoring of the arterial haemoglobin saturation (SaO_2) is useful for assessment of adequacy of arterial oxygenation. Oxygen-haemoglobin saturation curve describe the relationship of SaO_2 and PaO_2. The sigmoid shape of the oxygen-haemoglobin saturation curve is relatively maintained until PaO_2 falls below 60mmHg. After this, SaO_2 will tend to fall precipitously with further decreases in PaO_2. Calculated SaO_2 is typically provided as part of a blood gas analysis.

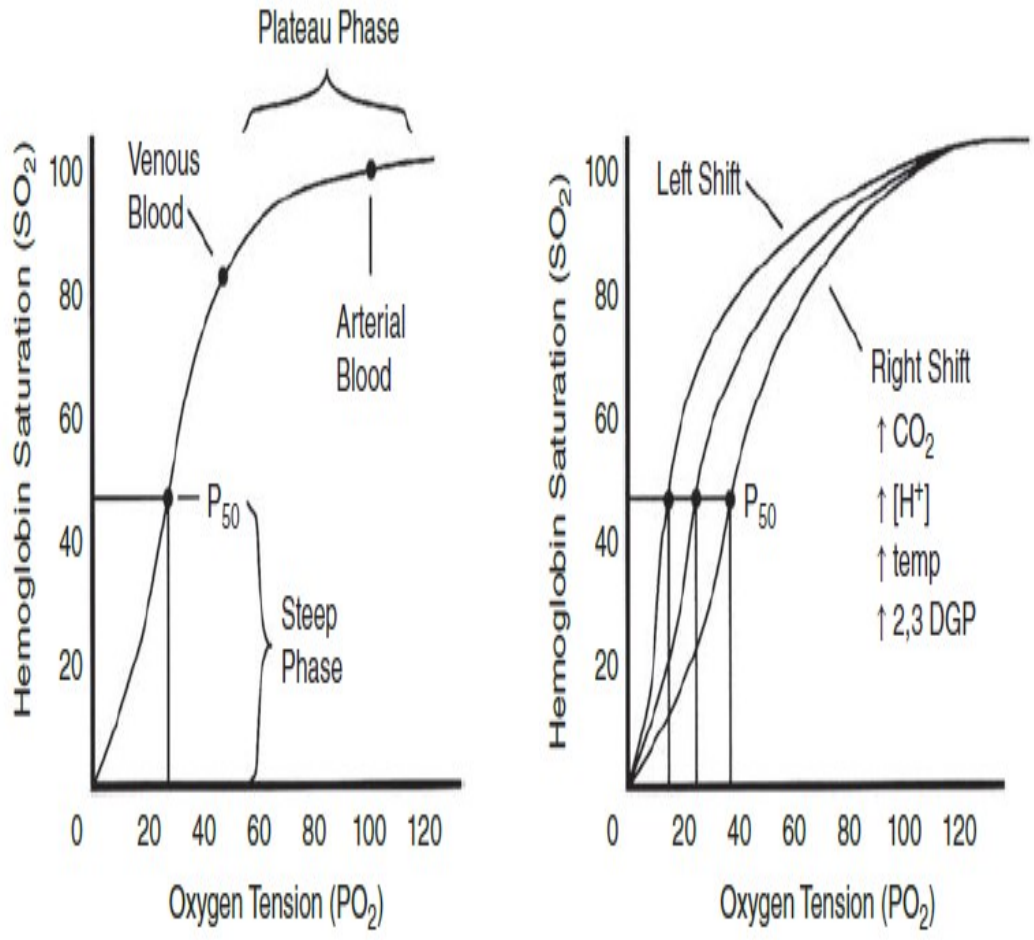

Figure 2.2: O_2haemoglobin curve

Pulse Oximetry

This is a device that uses calorimetry to estimate haemoglobin saturation in capillary beds. It relies on detection of pulsatile changes in haemoglobin saturation to estimate SaO_2. This can provide continuous data and it is non-invasive. It works best when the pulse pressures are normal to strong and less well when pulses are weak. The normal range for SaO_2 or SpO_2 in about 98-99%. Hypoxaemia occurs when oxygen-haemoglobin saturation is less than 95% and severe hypoxaemia occurswhen SpO_2 is less than 90% in animal patients.

Heart rate and rhythm

This is an important determinant of cardiac output (Q). Heart rate (beats per minute) in healthy animals is variable; 70-90bpm in small ruminants (Muir *et al*., 2013). Fluctuations in heart rate is a sensitive index of a change in the physiologic status of the animal patient.Excessive bradycardia diminishes cardiac output even though stroke volume (SV) may increase due to longer diastolic filling times. Excessive tachycardia can diminish Q due to shortened diastolic filling time and reduces stroke volume. (Haskin,2005). The reasons for reduced heart rate include anaesthetic agents, increased vagal tone, and metabolic disorders such as hypovolaemia, hypoxaemia, hypercapnia, hyperthermia, post-operative pain and heart diseases (Riebold, 2007).

In animals, tachycardia is a major concern as it impacts on diastolic filling and whether it is related with ventricular arrhythmia. Conservative intervention trigger level is estimated to be >100bpm for small ruminants. Also, tachycardia should be evaluated when there is evidence of poor cardiac output,hypotension and poor perfusion (Haskin and Pascoe, 1986)

Arterial Blood Pressure

Although, mathematical expressiondoes not depict oxygen delivery, it is most times assessed to evaluate changes in cardiac output (Mazzaferro and Wagner, 2001).The mean arterial or perfusion pressure (MAP) is the preferred pressure of perfusion as more time in the cardiac cycle is spent closer to MAP than to systolic arterial pressure. It is the product of cardiac output and systemic vascular resistance. Cardiac output is the product of heart rate and stroke volume, which is determined by coupling factors of preload, afterload and contractility (Saga *et al*., 1985; Mellema, 2001). The systolic

arterial pressure is the peak pressure, while diastolic arterial pressure is the least during the cardiac cycle; it is determined by stroke volume and arterial vascular compliance. The diastolic arterial pressure is the least pressure before the next heart beat and it is primarily determined by rate of diastolic run-off (vasomotor tone) and heart rate (Kallet *et al*., 1997).

The mean arterial pressure (MAP) is taken as pressure of perfusion as more time in the cardiac cycle is spent closer to MAP than SAP (Saga *et al*., 1985).Poor systolic function, impaired systolic efficiency, bradycardia and low systemic vascular resistance are traceable to hypotension and reduced venous return (Haskins, 2005).

2.9 Biological response to stress

Response to stress is an adaptive mechanism of neuroendocrine, metabolic, haematological and behavioural alterations designed to restore or maintain homeostasis. Stress produces useful outcomes that assist the animal patient to respond to harmful forces by activating various pathways such as glycolysis and glycogenolysis, which makes more glucose available for increase tissue metabolism (Desborough, 2000).

2.9.1 Mechanism of Stress

Physical restraint, anaesthetic, accidental or surgical trauma and emotional states (pain, fear and anxiety) initiate secretion of cytokines such as Interleukin-1, Interleukin-6 and tumour necrotic factor into the blood stream and also activation of corticotropin-releasing factor (CRF) in the brain, which activates the hypothalamic pituitary-adrenocortical axis and sympathetic nervous system (Breazile, 1987). Activation of the hypothalamus and anterior pituitary release adrenocorticotropic hormones (ACTH), vasopressin (or antidiuretic hormone, ADH), growth hormone and thyroid-stimulating hormone (TSH). Sympathetic nervous system and adrenal cortex activation initiates the release of epinephrine, norepinephrine, cortisol, aldosterone and renin (Barth *et al*., 2007). Together, these hormonal changes can alter haemodynamics, with increases in heart rate, blood pressure, cardiac output and coagulability of blood predisposing to thrombosis, increased metabolism and caloric requirements and when exaggerated, depress the immune function. The consequences of these hormonal changes are elevated catabolism, metabolization of substrates to produce energy for tissue repairs,

salt and water retention to maintain fluid volume and cardiovascular homeostasis (Breazile, 1987; Desborough, 2000).

2.9.2 Pathophysiology of Stress

An increase in the production of catabolic hormones promotes the availability of food substrates from the breakdown of carbohydrate, fats and proteins. The outcome of this is hyperglycemiaas a result of release of a protein hormone called glucagon and hypoinsulinaemia by the pancreas(Valverde and Doherty, 2008; McDonnell and Unpierrez, 2012). Breakdown of lipid is activated by adrenal cortex hormone, cortisol, catecholamine along with growth hormone, leading toupsurge of glucose and fatty acids in the blood.Consequently, secreted glycerol serves as substratefor gluconeogenesis in the liver. Also, protein catabolism is possible with the released cortisol, resulting into increased circulating amino acids making new proteins, more glucose and other substrates available in stressful conditions (Carli, 2014). The peripheral leucocyte count generally reflects a stress leucogram typified by an elevated number of mature and immature polymorphonuclear leucocytes (left shift) and reduced number of lymphocytes (Breazile, 1987; Yu *et al*., 2003). Chronic pain can produce prolonged elevation in the levels of several systemic hormones most especially the adrenocortical and medullary hormones, cortisol and catecholamines respectively (Desborough, 2000; Carli, 2014). Too much stress (distress) may produce negative haemodynamic changes, reduce glucose availability for tissue metabolism, impaired immune system, and prolonged wound healing (Muir, 1990; Finnerty *et al*., 2013)

2.9.3. Biomarker of Stress

Several physiological indicators have been used by researchers to evaluate stress levels in food animals. Stress causes plasma glucocorticoids to increase most of the time and they produce hyperglycaemia by increasing hepatic gluconeogenesis, inhibiting glucose uptake by the cells and enhancing lipid-protein catabolism. These effects may lead to ketosis, hyperlipaemia, hyperaminoacidaemia and metabolic acidosis (Taylor and Wheeler, 1996). In this regard, concentrations of plasma cortisol have been assessed in goats as a consistent indicator of short-term stress (Nwe *et al*., 1996). This steroidal hormone is produced by adrenal cortex in response to adrenocorticotropic hormone (ACTH) stimulation (Allen *et al.,* 2014).Fast increase in plasma cortisol secretion occurs following injury and this has been shown to be relateddirectly to the

magnitude of trauma (Hucklebridge *et al*., 1999; Desborough, 2000; Brook and Marshal, 2001). Cortisol promotes gluconeogenesis and protein catabolism resulting in the release of amino acids, which can be used either to form new proteins or to produce glucose and other substrates (Breazile, 1987; Desborough, 2000). It induces insulin-resistance, enhances lipolysis and has anti-inflammatory effect. However, anaesthetic drugs or sedatives can slow down the release of cortisol thus reduce the level ofcortisol in the plasma (Fragen*et al*., 1987; Sanhouri*et al*., 1992).

Stress-induced hyperglycaemia is an adaptive response, which mobilizes energy storesand behavioural changes in response to life-threatening conditions (Schmidt*et al*., 2010).The resultant hyperglycaemia is a direct outcome of an elevated level of catecholamines, cortisol, glucagon and growth hormone, which induce endogenous production of glucose via gluconeogenesis and glycogenolysis (Barth, 2007).In ruminants, glucose in the blood is stable because it isproduced mainly by gluconeogenesis instead of being derived from the gut directly. It has also been reported that there was reduced glucose concentrationin the blood after morning feeding of hay after which prefeeding level was restored within 2.5 hours (Eriksson and Teravainen, 1989).

Normally, glucose level is regulated through insulin-mediated glucose uptake in peripheral tissues (muscles and adipose tissue) and by liver (by GLUT2 receptor) and inhibition of hepatic glucose production (Celly *et al*., 2004; McDonnell and Umpierrez, 2012). During periods of stress, insulin resistance causes hyperglycaemia and muscle protein breakdown, which are consequences of severe stress response (Carli, 2014).

Lactate dehydrogenase (LDH)is an isoenzyme present in virtually all living cells and vital organ systems; its activity is abnormal in a many disease state and this varies from one animal species to another, it also depend on tissue distribution. It catalyses energy producing reaction in the cells (Goddard *et al*., 1997; Yu *et al*., 2001). Muscle, liver, and erythrocytes are the usual sources of high LDH activity in serum. In study carried out in deer undergoing stressful procedure to evaluate LDH activity, correlation was not recorded between cortisol concentration and LDH activity. This finding suggested 60-90minute duration of exposure to stress before appearance of LDH in plasma (Jones andPrice, 1992). In another study, release of LDH from cells invitro was

maximal within two hours post-injury (Ellis *et al*., 1995). In animals, increase in LDH activity is indicative of muscle damage and alteration in the activity of LDH can be broadly ascribed to physical stress rather than psychological stress (Goddard*et al*.,1997). To date, Serum LDH activity in goats is yet to be reported.

CHAPTER THREE

3.0 MATERIALS AND METHODS

This study was approvedby the Animal Care and Use Research Ethics Committee (ACUREC), University of Ibadan (UI-ACUREC/18/0029)

3.1 Animals

Six healthy bucks aged 1.5 to 2 years and having a mean body weight of 11±2.0kg were used for the research. They were bought from a local goat market in Ibadan and selection was based on signalment and normal physical examination findings. The selected goats were housed at the experimental unit of the Faculty of Veterinary Medicine in a communal goat pen with a concrete floor bedded with wood shavings. They were fed a basal diet of star grass (*Cyanodonalaniferensis*) and cassava peels, additional cereal concentrate ration at a rate of 50g/head/day *ad libitum*. Salt lick and fresh, clean water were provided ad libitum. A period of one month was allowed for the goats to acclimatize to their new housing, feeding regimen and handling. Just before the start of the trials, the health status was evaluatedby complete blood cell count, haematocrit, plasma proteins and electrolytes assessments.

3.2 Drugs

The drugs used in the research consisted of:

i. Xylazine hydrochloride (Xylased ® Bioveta Laboratory, Ivanovice na Hane Czech Republic) supplied as a 20mg/ml solution for injection in a 50ml multidose vial
ii. Acepromazine maleate (ACP injection, Novartis Animal Health UK Ltd) marketed as a 20mg/ml solution for injection in a 20mls multidose vial
iii. Midazolam hydrochloride (Midazolam Hamelin Pharm. Ltd Glaucester, UK) supplied as a 50mg/ml solution for injection in a 2ml glass ampoule.

3.3 Research Design

The research design used comprised of prospective, randomized crossover experimental trials, carried out on sedated goats. A crossover design is a repeated measurement in which the (entire) whole sample size is used (and moved) from one treatment to another during the course of the trial using an appropriate washout effect to eliminate the impact of carryover effect. This is in contrast to a parallel design in which animals are randomized to a treatment and remain on that treatment throughout the duration of the trial. A crossover design usually yields more efficient comparison than parallel design because each animal serves as its own matched control. Furthermore, fewer animals may be required in crossover design in order to attain same level of statistical precision as a parallel design, minimum sample size for crossover design is five (Siyasinghe and Sooriyarachi, 2011).

Based on the three classes of sedative drugs employed, three main studies were carried out each consisting of five trials. In each trial, each of the six bucks was sedated and positioned for an hour in appropriate positions based on the trial in use. During this sedation, vital parameters were taken using the patient monitor at 10-minute interval for an hour. Blood samples were also collected before and after positioning and sent to the laboratory for analysis. Each trial took a week as a buck went through the experiment per day. Thereafter, thebucks were rested for 14 days in between clinical trials to allow for the wash-out of the sedative drugs. This was repeated for each study till all the trials were carried out, this is further illustrated in Table 3.1.

Table 3.1: Research design for the three classes of sedatives

Study	**Trial**	**Body Position**
Study I (Xylazine-sedated goats) (n = 6)	Trial 1	Standing (STP)
	Trial 2	Right-lateral (RL)
	Trial 3	Left-lateral (LL)
	Trial 4	Supine (SUP)
	Trial 5	Prone (PP)
Study II (Acepromazine-sedated goats) (n = 6)	Trial 6	Standing (STP)
	Trial 7	Right-lateral (RL)
	Trial 8	Left lateral (LL)
	Trial 9	Supine (SUP)
	Trial 10	Prone (PP)
Study III (Midazolam-sedated goats) (n = 6)	Trial 11	Standing (STP)
	Trial 12	Right-lateral (RL)
	Trial 13	Left lateral (LL)
	Trial 14	Supine (SUP)
	Trial 15	Prone (PP)

3.4 Experimental Procedure

At the start of each trial, the body weight of each goat was determined using bathroom scale for calculating drug dosage. A total of 5ml whole blood each was collected from the jugular vein into lithium heparin sample tube to determine baseline values of Cortisol and LDH. Another 5mls of blood was collected into sodium fluorine EDTA sample tube to determine baseline values of glucose. Another sample was taken at the end of an hour for determination of cortisol, LDH and glucose. The goat was administered sedative agent at recommended clinical doses of 0.05mg per kg xylazine, 0.2 mg per kg acepromazine or 0.3mg per kg midazolam as appropriate (Clarke *et al*., 2014). All drugs were injected intramuscularly in the femoral muscle of the goats. The sedated goat was then restrained as appropriate in a chosen body position, which includedstanding, supine and prone positions with the aid of constructed specialized chute that also stabilized the heads. Right and left lateral positions were achieved with aid of an operating table. The standing position was used as control. The goat was maintained in a body position for one hour.

TheStanding Position

Figure 3.1 is illustrating sedated goat in standing position. Thisposition was achieved using a fabricated chute, to facilitate the stability of sedated goat in this posture during the clinical trial. Also, the head was maintained in stable position using additional attached soft surface to the chute. The abdominal region of the sedated goat was allowed to rest onsoft gauze, which was attached across the chute during standing positioning.

Figure 3.1: Standing position (STP)

TheRight-Lateral Position

Figure 3.2 is showing sedated goat placed in right-lateral recumbency. Thisposition was made possible with the aid of an operating table. The head of the sedated goat was flexed slightly to prevent aspiration of saliva or ruminal content during positioning. Also, this facilitated easy attachment of monitor clips for assessment.

Figure3.2: Right-lateral position (RL)

The Left-Lateral Position

Figure 3.3 is showing sedated goat placed in left lateral recumbency. The operating table was used to achieve this position. Aspiration of copious saliva or ruminal content during sedation was prevented by slight flexion of the head while the animal was placed in this position. The monitor apparatus was attached easily with these precautions.

Figure 3.3: Left-lateral position (LL)

TheSupine Position

Figure 3.4 is illustrating sedated goat placed in dorsal recumbency (also known as supine position). This positioning was facilitated with the aid of fabricated chute. The limbs of the sedated goat were attached using gauze and slip-knot tie, to maintain the animal in stable position. This also aided in attachment of monitor clips with ease throughout the period of clinical trials.

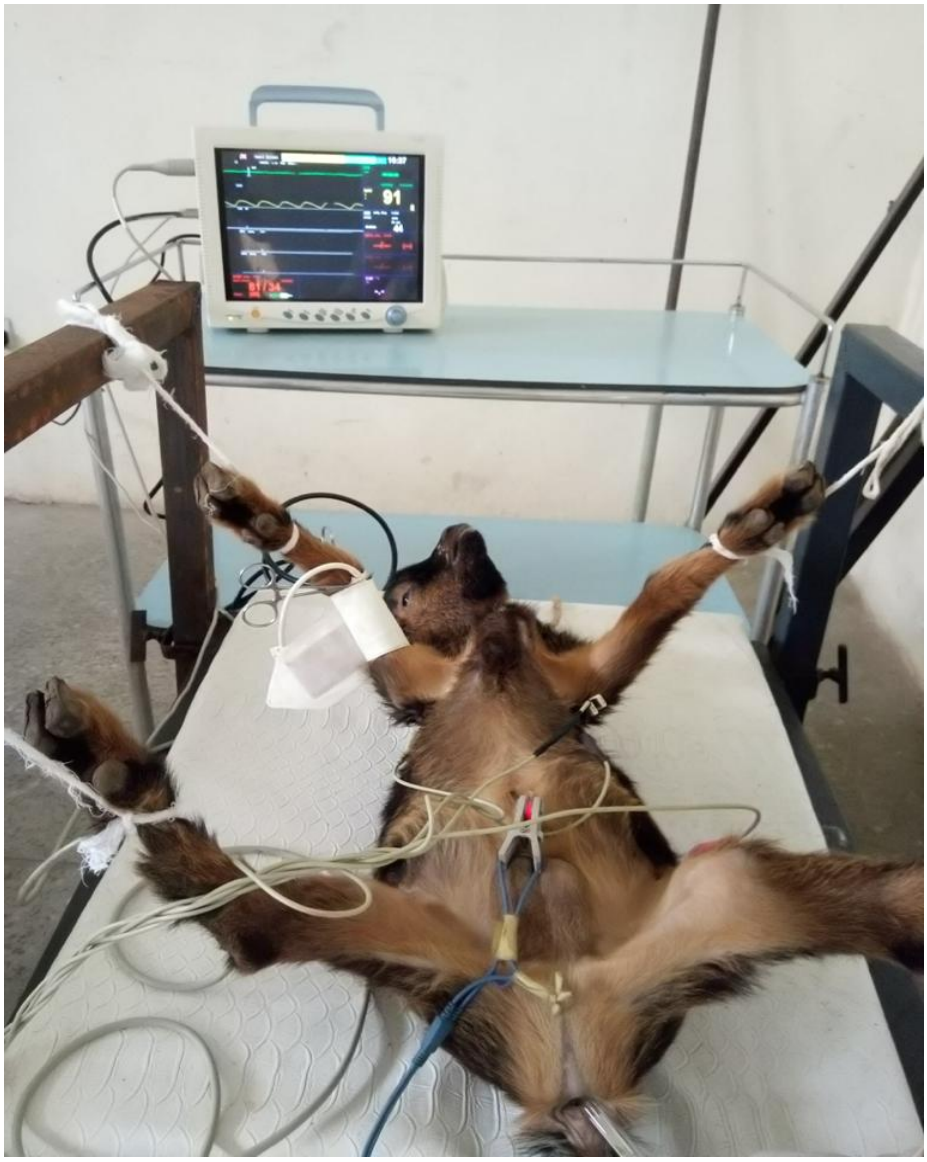

Figure 3.4: Supine position (SUP)

TheProne Position

Figure 3.5 is showing sedated goat in sternal recumbency (also known as prone position).Positioning was achieved using the fabricated chute. The head was maintained in stable position by resting the chin on the anterior attachment of the chute throughout the clinical trial. This also aided in easy attachment of the montor clips.

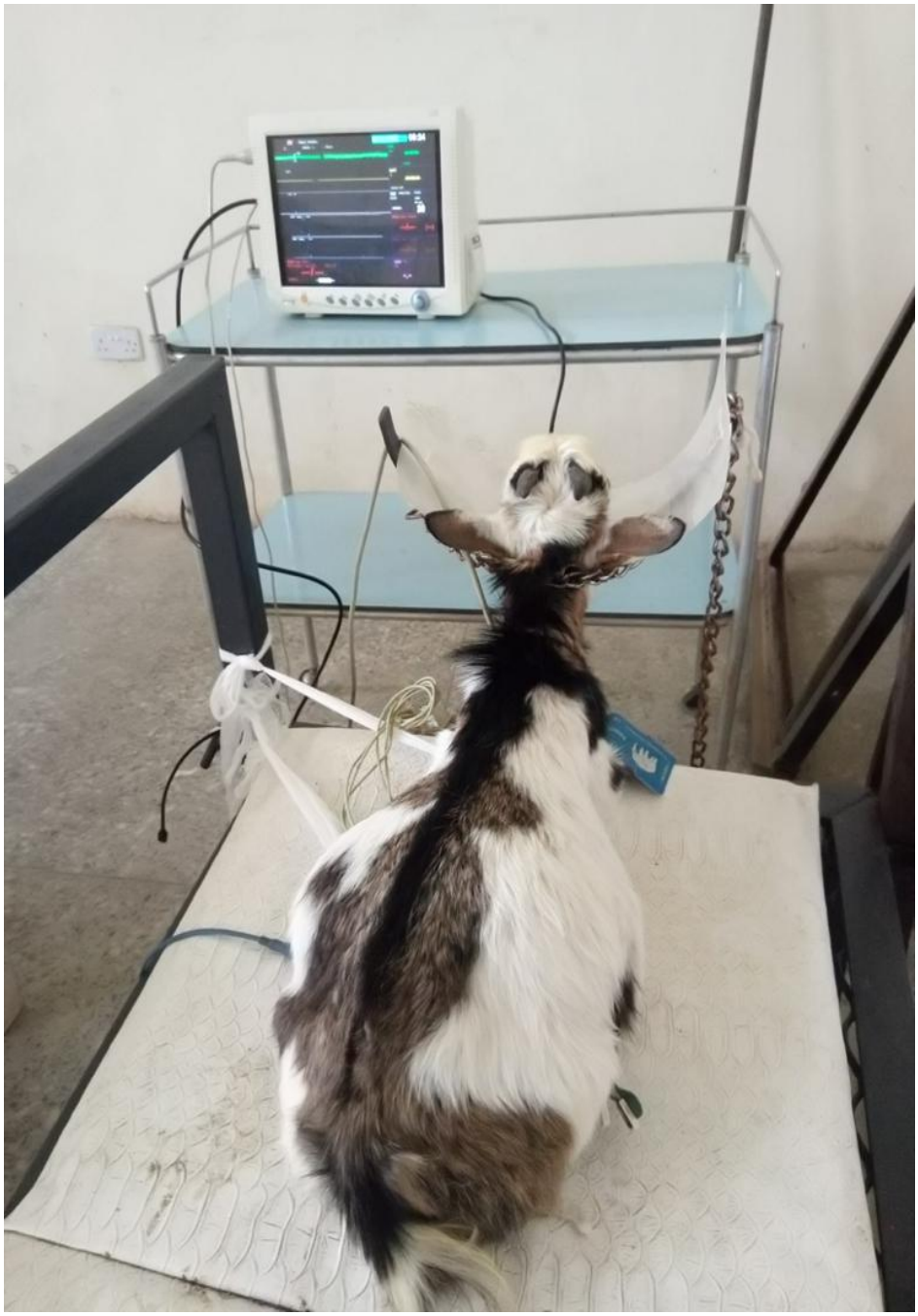

Figure3.5: Prone position (PP)

3.5 Physiological Measurement

The restrained sedated goat was attached to a veterinary multiparameter patient monitor (Cardell® 9500HD) for measurement of physiological variables. Heart rate (HR) in beats/minutes, respiratory rate (RR) in breath/minute, mean arterial pressure (MAP) in mmHg, and oxygen saturation (SpO_2) in percentage (%) were recorded. Rectal temperature (RT) in ˚C was measured using an electronic thermometer. All measurements were taken immediately and during maintenance of body position at 10minutes intervals over a period of one hour.

3.6 Laboratory Analyses

Blood samples collected in tubes were sent to a specific laboratory at the University College Hospital, Ibadan on ice pack for the analysis for three stress biomarkers; glucose, cortisol and lactate dehydrogenase (LDH).

3.6.1 Determination of Plasma Glucose

The Glucose HK Gen. 3 Kit (GLU3, Roche Diagnostics GMbH Sandfofer Strasse 116 D-68305 Manheim, Germany) was used for plasma glucose analysis. It uses the UV test, which is enzymatic reference method with hexokinase (Hexokinase catalyzes the phosphorylation of glucose to glucose-6-phosphate by ATP). Glucose + ATP → G-6-P + ADP. Glucose -6-Phosphate dehydrogenase oxidizesglucose-6-phosphate in the presence of NADP to gluconate-6-phosphate. No other carbohydrate was oxidized. The rate of NADPH formation during the reaction was directly proportional to the glucose concentration and was measured photometrically. The equipment used was cobas c311 by Roche and it was done on the cobas auto analyser.

3.6.2 Determination of Plasma Cortisol

The ARCHITECT Cortisol Reagent Kit (Abbott) Laboratories Diagnostics Division by Fisher Diagnostics, a division of Fisher Scientific Company LLC, 8365 Valley Pike, Middle town, VA 22645-1965, USA) was used to determine the plasma cortisol activity. This was done on Abbott i1000SR (auto analyses). The ARCHITECT Cortisol assay is a delayed one-step immunoassay for the quantitative determination of cortisol in serum or plasma using CMIA technology with flexible assay protocol referred to as Chemiflex. The samples collected were combined with anti-cortisol paramagnetic

micro particles. The cortisol present in the sample binds to the anticortisol coated microparticles. After incubation, cortisol acridinium-labeled conjugate was added to the mixture. Following a second incubation, the micro particles were washed and pre-trigger and trigger solutions were added to the reaction mixture. The resulting chemiluminescent reaction was measured as relative light unit (RLUS). There was an inverse relationship between the amount of cortisol in the sample and the RLUS detected by the ARCHITECT iSystem optics.

3.6.3. Determination of LDH

Lactate dehydrogenase in the sample was analysed using Lactate HK Gen3. (LDH3, Roche diagnostics GmbH Sandhofor Strasse 116 D-68305 Mannheim, Germany). The principle of LDH estimation is optimized standard method according to the Deutsche Gesellscaft fur Klinische Chemie (DGKC). LDH catalyzes the reaction between pyruvate and NADH to form L-lactate and NAD^+; Pyruvate + NADH + H^+LDH L-lactate + NAD^+. The initial rate of the NADH oxidation is directly proportional to the catalytic LDH activity. It was determined by measuring the decrease in absorbance at 340nm. The LDH analysis was auto analysed using cobas c311 by Roche using the above principle.

3.7 Statistical Analysis

The data generated were analysed statistically using the PRISM Software package (version 5.0 Graph pad Software Inc, San Diego CA, USA). Where applicable, all data were expressed as mean ± standard deviation (SD). The physiological variables (HR, RR, MAP, SPO_2, RT) were compared using analysis of variance (ANOVA) and student's t-test was used to assess statistical significance for paired data (Stress markers; Glucose, Cortisol and LDH). Values of probability less than 5% ($\alpha_{0.05}$) were considered significant for all data.

CHAPTER FOUR

4.0 RESULTS

4.1 Responses of xylazine-sedated goats

In all the five trials involving xylazine, the sedative agent produced cooperative animals that did not resist head and rope restrain. The sedated goats salivated for the first 10 minutes. All laterally recumbent sedated goats developed transient ruminal tympany due to their inability to eructate. Xylazine induced good muscle relaxation, which facilitated body positioning of the experimental goats. Cardiopulmonary responses of xylazine-sedated goats to STP, RL, LL, SUP and PP are shown in Figures 4.1.1 – 4.1.5.

4.1.1 Responses of xylazine-sedated goats to STP, right-lateral, left- lateral, supine and prone positions

Cardiopulmonary responses of xylazine sedated goats to standing (STP), right-lateral (RL), left-lateral (LL), supine and prone positions are shown in Table 4.1.1. The ranges of mean HR in the STP were 66.0±13.4 to 78.6±31.4 beat/min, in the RL from 63.8±11.0 to 65.7±9.4 beat/min and from 59.5±8.2 to 63.0±8.2 beat/min in LL. In SUP, HR ranged from 60.0±3.6 to 66.7±14.7 beat/min and from 69.0±11.7 to 77.7±11.3 beat/min in PP.MAP in STP ranged from 61.3±10.1to 69.7±13.8mmHg, from 45.3±19.5 to 58.0±10.1mmHg in RL and from 49.2±3.8 to 55.5±13.8mmHg in LL. The ranges of MAP in SUP were from 43.5±10.4 to 66.2±10.3mmHg and from 57.0±12.1 to 65.5±5.7mmHg in PP.Mean RR in STP ranged from 23.2±6.8 to 30.3±13.9 breath/min, from 25.8±10.9 to 31.3±9.5 breath/min in RL and 23.5±13.9 to 37.2±18.9 breath/min in LL. Mean RR in SUP ranged from 24.2±11.3

to 37.0±10.8 breath/min and 18.2±6.5 to 27.3±7.0 breath/min in PP.The ranges of SPO_2 in STP were from 88.3±4.7 to 93.7± 2.7%, from 79.3±34.7 to 96.7±2.3% in RL and from 86.5±10.2 to 91.8±6.5% in LL. The ranges of SpO_2 in SUP were from 89.5±2.1 to 91.5±5.1% and 85.8±7.2 to 95.1±4.1% in PP.Mean RT ranged from 37.8±0.3 to 39.0±0.2°C in STP, from 36.7±0.6 to 39.0±0.3°C in RL and from 36.6±0.6 to 38.3±0.5°C in LL.The RT ranged in SUP from 37.3±0.8 to 38.6±0.6°C and 38.0±0.5 to 38.8±0.3°C in PP.

Table 4.1.1: Cardiopulmonary responses of xylazine-sedated goats to STP, RL, LL, SUP and PP

Para Meters	Position	Time Interval (minutes)						
		0	10	20	30	40	50	60
HR (beats/ min)	STP	78.6 ± 31.4	72.4 ± 23.4	69.6 ± 19.4	69.7 ± 1.6	68.7 ± 17.1	66.0 ± 13.4	70.3 ± 14.8
	RL	65.0 ±5.8*	65.0 ± 7.0	65.7± 9.4	64.7 ± 15.5	64.2 ± 15.5	63.8 ± 11.0	65.5 ± 13.4
	LL	61.7 ± 9.6*	59.5 ± 8.2*	61.3 ± 10.7	61.8 ± 11.1	60.2 ±10.9	62.3 ± 10.9	63.0 ± 8.2
	SUP	60.0 ± 3.6*	60.7 ±4.5	60.8± 5.2	60.3 ± 7.3	66.7 ± 9.6	66.7 ± 14.7	62.5 ±9.9
	PP	77.7 ± 11.3	74.3 ± 13.8	72.7 ± 13.8	72.3 ± 11.4	70.8 ± 13.2	69.0 ± 11.7	70.0 ± 10.0
MAP (mmHg)	STP	61.3 ± 10.1	66.8 ± 13.4	69.7 ± 13.8	66.7 ± 5.8	66.8 ± 7.19	66.8 ± 10.8	66.0 ± 6.4
	RL	52.5 ± 6.7	55.8 ± 5.4	51.3 ± 6.8*	45.3 ± 19.5*	53.5 ± 7.5	58.0 ±10.1	54.2 ± 3.3*
	LL	54.0 ± 7.2	51.7 ± 5.4*	50.7 ± 6.3*	50.7 ± 5.8*	49.2 ± 3.8	54.8 ± 5.4*	55.5 ± 3.8*
	SUP	43.5 ± 10.4*	45.2 ± 6.1*	49.2 ± 10.2*	53.8 ±11.5*	56.8 ± 8.4	62.3 ± 8.6	66.2 ±10.3
	PP	64.8 ± 12.1	63.7 ± 12.2	57.0 ± 12.1	63.2 ± 10.8	60.0 ± 7.1	59.0 ± 10.4	65.5 ±5.7
RR (breaths/ min)	STP	27.0 ± 8.5	24.8 ± 6.2	23.2 ± 6.8	25.3 ± 7.8	24.8 ± 7.8	27.0 ± 10.1	30.3 ±13.9
	RL	31.3 ± 9.5	29.2 ± 5.0	26.0 ± 5.2	30.5 ± 11.6	29.7 ± 13.2	25.8 ± 10.9	26.0 ± 11.6
	LL	30.7 ± 15.5	26.3 ±9.6	26.2 ± 12.5	23.5 ± 13.9	29.8 ± 16.5	31.8 ±15.2	37.2 ±18.9
	SUP	28.0 ± 7.6	27.5 ±9.5	24.2 ±11.3	27.7 ±11.5	37.0 ± 10.8	29.3 ± 11.8	31.7 ± 9.4
	PP	24.5 ± 2.6	21.7 ± 5.8	18.2 ± 6.5	27.3 ± 7.0	25.3 ±6.6	24.8 ± 6.1	25.7 ± 7.0
SPO_2(%)	STP	93.7 ± 2.7	92.2 ± 4.5	88.8 ± 4.8	88.3 ± 4.7	90.5 ± 7.9	91.3 ± 5.7	93.3 ± 4.1
	RL	94.5 ± 3.8	94.5 ± 3.3	96.7 ± 2.3	95.0 ± 2.6	94.8 ± 2.6	79.3 ± 34.7	93.7 ±3.9.
	LL	86.5 ± 10.2	89.3 ± 10.2	89.0 ± 7.0	91.8 ± 6.5	91.2 ± 5.2	90.2 ± 4.2	89.7 ± 5.5
	SUP	91.2 ±4.4	90.7 ± 6.0	89.5 ± 4.3	91.3 ± 2.0	91.3 ± 2.5	91.5 ± 5.1	89.5 ± 2.1
	PP	87.2 ± 6.7	91.5 ± 5.8	85.8 ± 7.2	91.5 ± 5.5	95.1 ± 4.1	92.2 ± 4.0	93.0 ±3.5
RT ˚C	STP	39.0 ± 0.2	38.8 ± 0.2	38.7 ± 0.2	38.4 ± .0.2	38.2 ± 0.3	38.1 ± 0.3	37.8 ±0.3
	RL	39.0 ±0.3	38.1 ± 0.5	37.8 ±0.5	37.5 ± 0.4	37.2 ± 0.4	36.7 ± 0.6	36.8 ± 0.5
	LL	38.3 ± 0.5	37.7 ± 0.5	37.3 ± 0.6	37.2 ± 0.7	37.0 ± 0.8	36.7 ± 0.6	36.6 ± 0.6
	SUP	38.6 ± 0.6	38.1 ± 0.5	37.8 ± 0.6	37.7 ± 0.6	37.6 ± 0.7	37.5 ± 0.7	37.3 ± 0.8
	PP	38.8 ± 0.3	38.7 ± 0.3	38.6 ± 0.2	38.5 ± 0.3	38.3 ± 0.3	38.4 ± 3.4	38.0 ± 0.5

Superscript (*) indicates significant ($p<0.05$) decrease compared with the standing position
Data are expressed as Mean ± SD of sixgoats
MAP: Mean Arterial Blood Pressure RR: Respiratory Rate
HR: Heart Rate SPO_2: Oxygen-saturation
RT: Rectal Temperature

4.1.1 Cardiopulmonary Responses

Mean HR of xylazine-sedated goats for STP, RL, LL, SUP and PP were compared in Figure 4.1.1. Compared to the STP, mean HR were significantly ($p<0.05$) lower in RL, LL and SUP positions, the mean HR in PP was not significantly ($p>0.05$) different from the STP. Similarly, MAP in the RL, LL and SUP were significantly ($p<0.05$) lower than that in STP. Only the MAP in the PP was not significantly ($p>0.05$) different from the STP. There were no significant ($p>0.05$) differences in the mean respiratory rate, oxygen-haemoglobin saturation, and rectal temperature of xylazine-sedated goats in RL, LL, SUP and PP compared to the STP values.

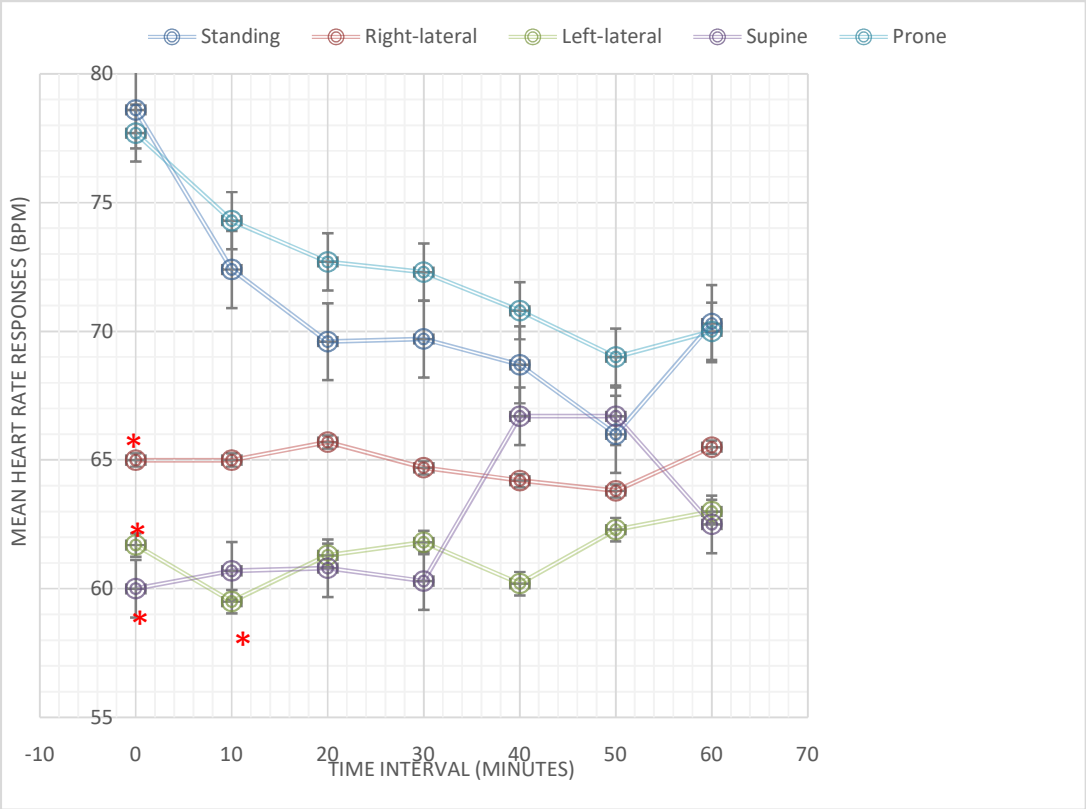

Figure 4.1.1: Comparison of the Heart Rate responses of xylazine-sedated goats to STP, RL, LL, SUP and PP

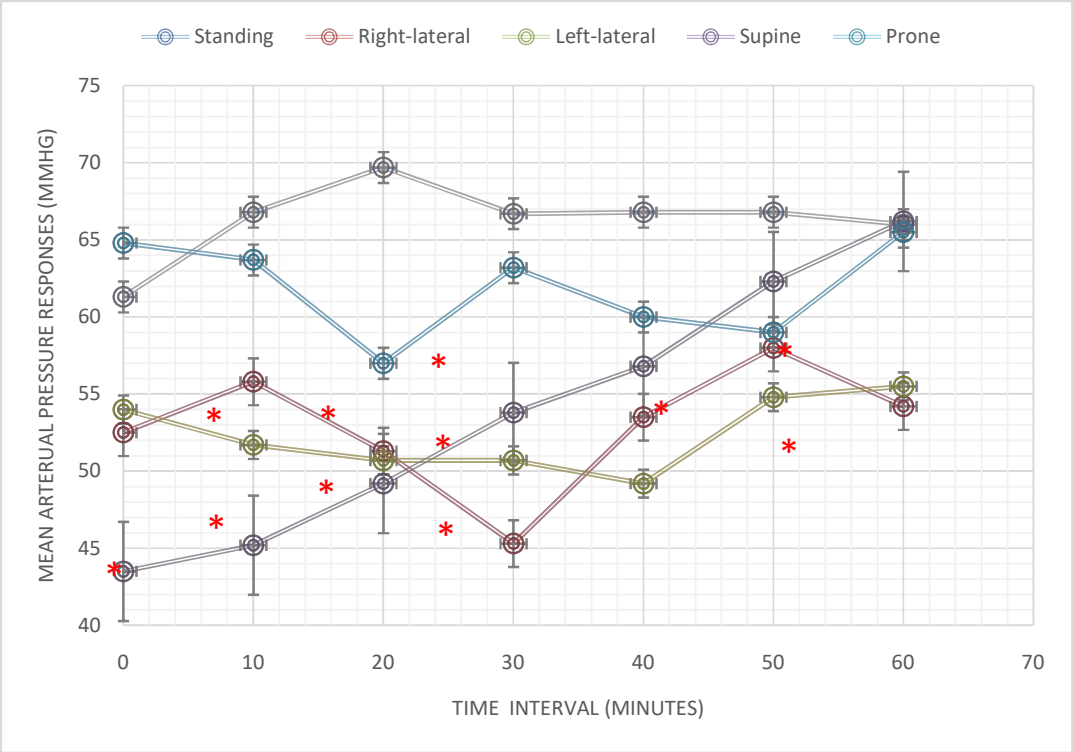

Figure 4.1.2: Comparison of the Mean Arterial Pressure responses of xylazinesedatedgoats to STP, RL, LL, SUP and PP

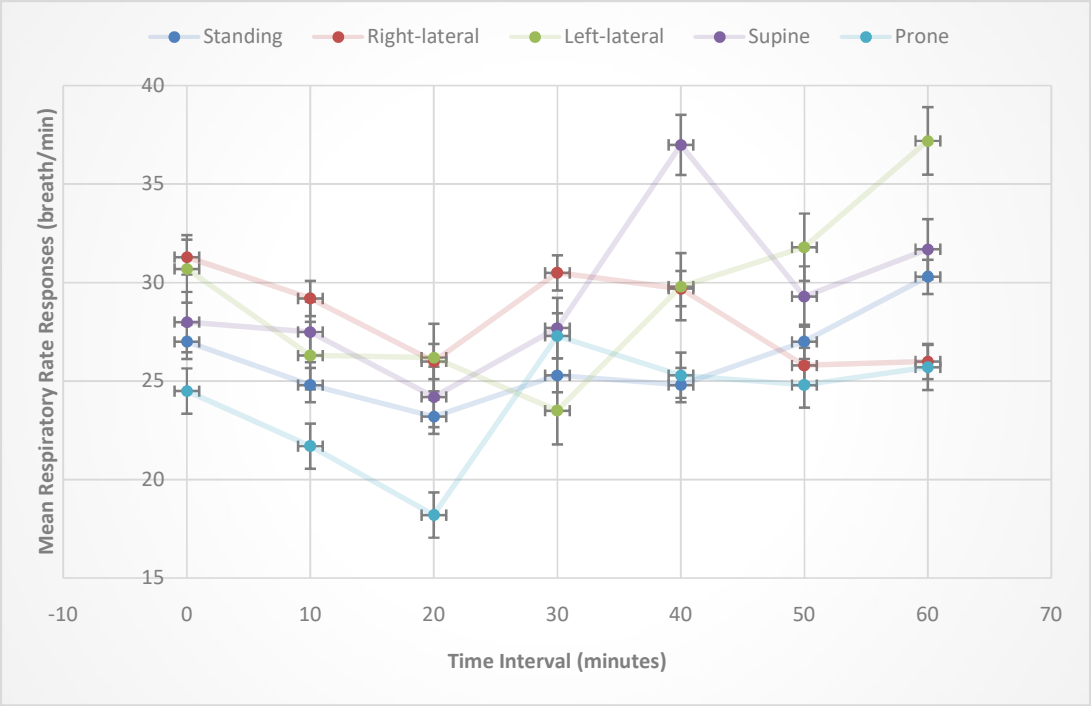

Figure 4.1.3: Comparison of the respiratory rate responses of xylazine-sedated goats to STP, RL, LL, SUP and PP

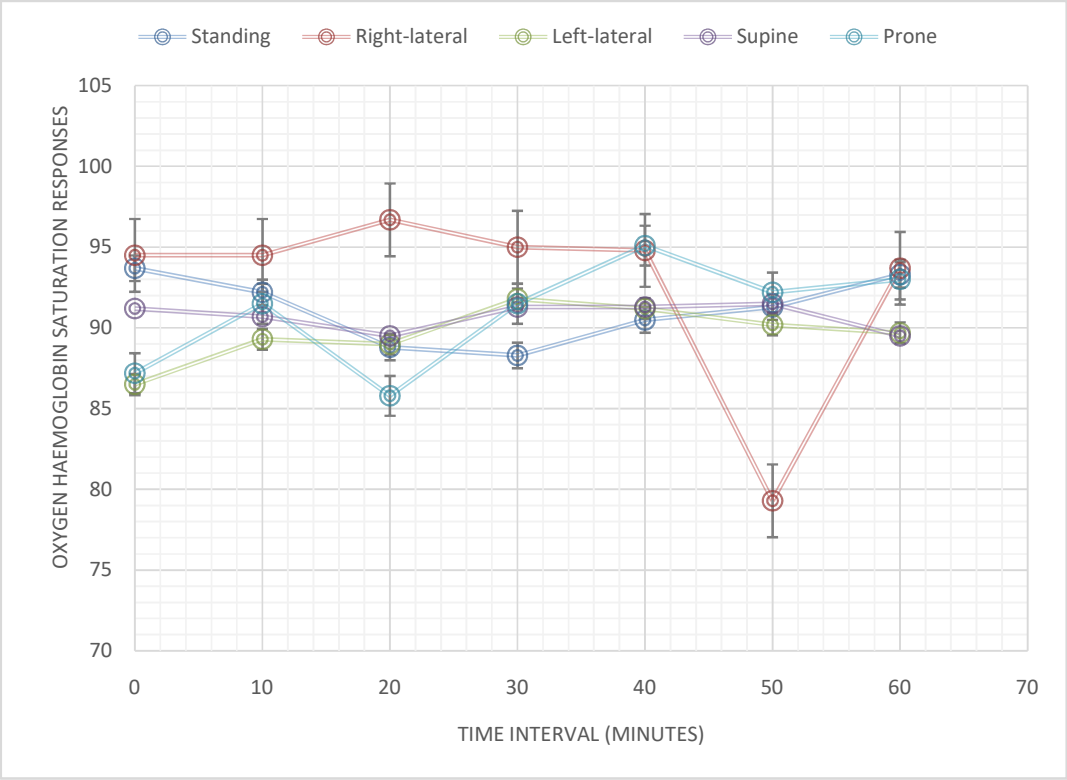

Figure 4.1.4: Comparison of the oxygen saturation (%) responses of xylazine- sedated goats to STP, RL, LL, SUP and PP

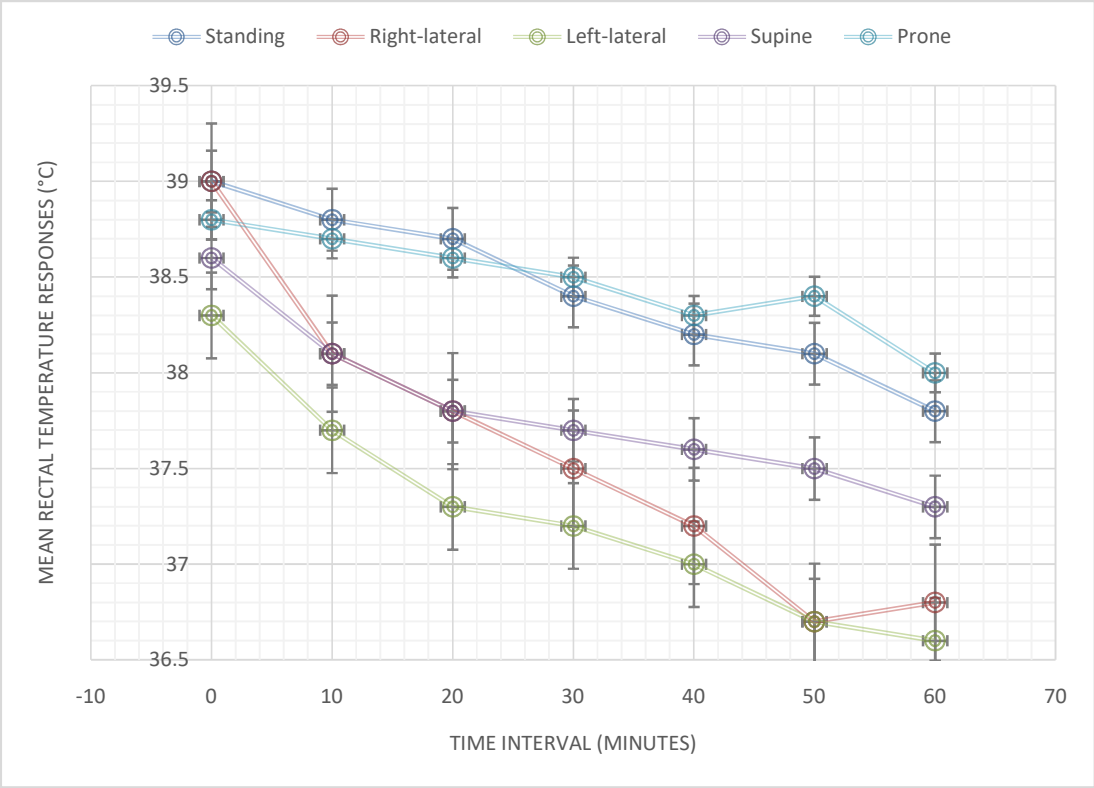

Figure 4.1.5: Comparison of the rectal temperature responses of xylazine-sedated goats to STP, RL, LL, SUP and PP

4.2 Stress Responses

Plasma cortisol responses of xylazine-sedated goat to all the studied body positions are shown in Figure 4.2.1 Mean plasma cortisol levels at 60 minutes rose above corresponding baseline levels for STP, RL, LL, SUP, and PP. After 60 minutes, mean plasma cortisol levels were significantly ($p<0.05$) higher in RL, SUP and PP than in STP.

Mean blood glucose responses of xylazine-sedated goats to all the studied body positions are shown in Figure 4.2.2 at 60 minutes, mean blood glucose levels rose above the corresponding baseline levels for STP, RL, LL, SUP and PP. Mean blood glucose levels were significantly ($p<0.05$) higher in RL and PP than STP. Mean values for LL and SUP were not significantly ($p>0.05$) different than the STP value.

The mean plasma LDH values of xylazine-sedated goats to all the studied body positions are shown in figure 4.2.3 Except for STP, mean plasma LDH levels for RL, LL, SUP and PP were lower than the corresponding baseline values and the corresponding baseline values and also significantly ($p<0.05$) lower than in STP.

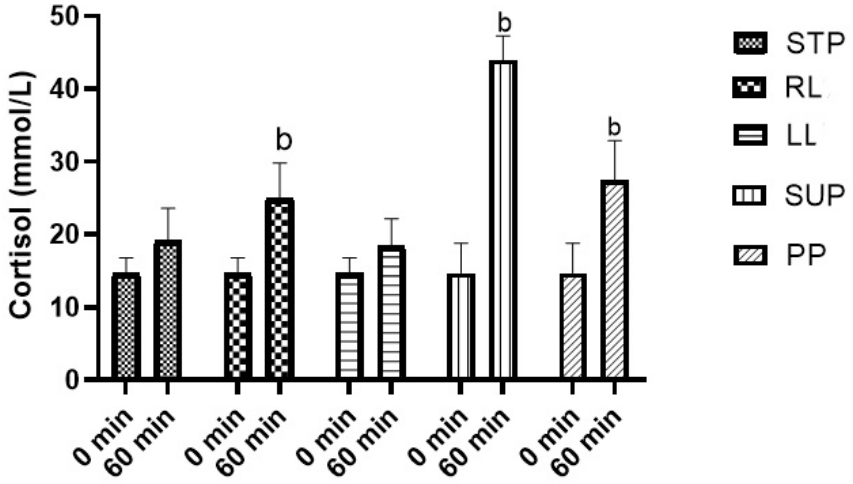

Figure 4.2.1: Cortisol level of xylazine-sedated goats to body positions. Superscript (b) indicates significant ($p<0.05$) increase compared with standing position. STP = standing position; RL = right lateral position; LL = left lateral position; SUP = supine position; PP = prone position

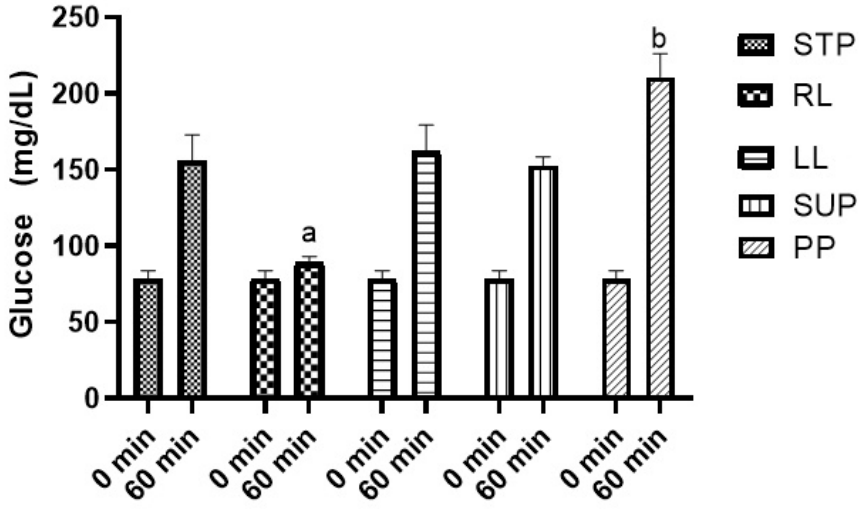

Figure 4.2.2: Glucose level of xylazine-sedated goats to body positions. Superscript (a) indicatessignificant ($p<0.05$) decrease compared with standing position; (b) indicates significant ($p<0.05$) increase compared with standing position. STP = standing position; RL = right lateral position; LL = left lateral position; SUP = supine position; PP = prone position

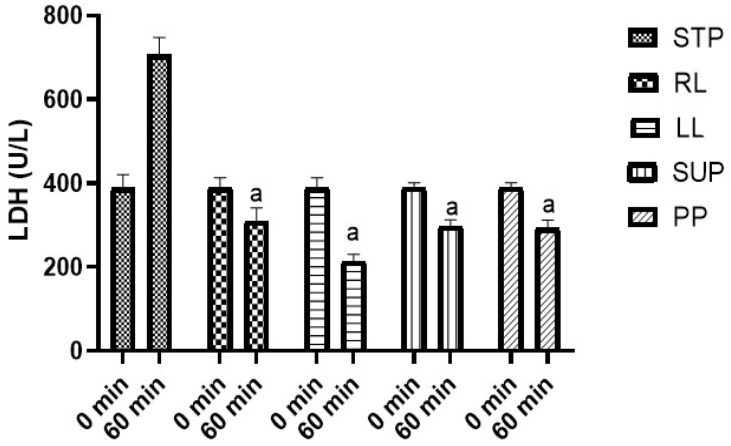

Figure 4.2.3: Lactate dehydrogenase level of xylazine-sedated goats to body positions. Superscript (a) indicates significant ($p<0.05$) decrease compared with standing position;. STP = standing position; RL = right lateral position; LL = left lateral position; SUP = supine position; PP = prone position

4.3 Responses of acepromazine-sedated goats

4.3.1 Acepromazine Sedation

In all the five trials involving acepromazine, the sedative agent produced pliable animal that tolerated head and rope restrain. Sedation produced only mild muscle relaxation with penile prolapse and no ruminal tympany or salivation was observed. In addition, no oesophageal reflux occurred. Cardiopulmonary responses of acepromazine-sedated goats to STP, RL, LL, SUP and PP are shown in (Table 4.3.1).

4.3.1: Responses of acepromazine-sedated goats to standing, right-lateral, left-lateral, supine andprone positions.

Cardiopulmonary responses of acepromazine are shown in Table 4.3.1. The mean HR in STP ranged from 123.7±24.0 to 136.7±31.7 beat/min, in the RL from 113.6±15.6 to 126.8±11.0 beat/min, and from 110.5±12.9 to 124.0±11.1 beat/min in LL. The mean HR in SUP ranged from 110.3±14.0 to 134.7±18.8beat/min and from 103.2±21.6 to 113.3±26.5 beat/min in PP.MAP of sedated goats in STP ranged from 67.7±33.5 to 87.0±10.7mmHg, from 56.7±5.9 to 70.0±10.5mmHg in RL, and from 57.3±11.6 to 64.5±18.6mmHg in LL.The recorded MAP ranged from 42.0±10.6 to 62.5±22.3mmHg in SUP, and from 73.2±9.8 to 82.2±8.8mmHg in PP. The ranges of RR in STP were from 25.2±6.2 to 31.2±7.5 breath/min, from 22.8±3.6 to 26.7±4.0 breath/min in RL and from 23.3±1.5 to 28.3±5.6 breath/min in LL.The ranges of RR in SUP were from 24.8±6.0 to 28.2±2.2 breath/min and from 25.5±3.2 to 30.8±4.0 in PP. SPO_2 in STP ranged from 87.0±6.1 to 91.3±.8%, in the RL from 91.5±6.4 to 95.2±3.8% and from 89.7±8.6 to 94.2±5.7% in LL. SPO_2in SUP ranged from 91.2±7.6 to 94.3±3.9% and from 89.8±5.2 to 94.3±3.1% in PP. Mean RT in STP ranged from 38.4±0.4 to 38.8±0.4°C, from 37.9±0.4 to 38.8±0.3°C in RL and from 37.2±1.1 to 38.0±1.1°C. Mean RT in SUPranged from 38.0±0.7 to 38.5±0.7°C and from 38.6±0.5 to 38.8±0.5°C in PP.

Table 4.3.1: Cardiopulmonary responses of acepromazine-sedated goats to STP, RL, LL, SUP and PP

Para Meters	Position	Time Interval (minutes) 0	10	20	30	40	50	60
	STP	128.7 ± 27.8	132.3 ± 29.6	123.7 ± 24.0	131.3 ± 26.8	136.3 ± 33.1	136.7 ± 31.7	134. 7 ± 35.6
HR	RL	126.8 ± 11.0	115.2 ± 17.1	122.0± 12.8	113.6 ± 15.6	118.8 ± 16.3	122.0 ± 14.2	125.4 ± 11.7
(beats/	LL	110.5 ± 12.9*	110.7 ± 43.2*	124.0 ± 11.1	111.2 ± 11.0*	115.0 ± 16.8	113.0 ± 9.3	118.5 ± 17.8
min)								
	SUP	110.3 ± 14.0	113.33 ± 12.1	129.2± 13.6	115.3 ± 22.8	126.0 ± 18.8	131.3 ± 16.3	134.7 ± 18.8
	PP	105.7 ± 25.9	103.2 ± 21.6	110.8 ± 20.9	110.7 ± 27.9	110.7 ±27.9	113.0 ± 25.3	113.3 ± 26.5
	STP	86.8 ± 15.0	81.7 ± 13.8	78.8 ±9.8	70.8 ± 33.5	67.7 ± 33.5	87.0 ± 10.7	80.2 ± 7.2
MAP	RL	63.7 ± 16.4*	56.7 ± 5.9*	64.7 ± 13.6*	66.5 ± 9.7	68.0 ± 9.8	70.0 ± 10.5*	67.3 ± 6.5*
(mmHg)	LL	57.3 ± 11.6*	61.7 ±8.5*	58.2 ± 10.3*	64.5 ± 18.6	60.2 ± 6.3	64.2 ± 17.8*	61.5 ± 15.2*
	SUP	54.2 ± 11.1*	55.7 ± 7.5*	53.3 ±9.4*	57.5 ± 11.4	49.2 ± 12.8	42.0 ± 10.6*	62.5 ± 22.3*
	PP	82.2 ± 8.8	79.2 ± 8.7	78.3 ± 8.4	79.8 ± 7.0	73.2 ± 9.8	78.2 ± 10.4	79.2 ± 5.6
RR	STP	27.7 ± 7.3	31.2 ± 7.5	25.2 ± 6.2	27.33 ± 6.0	29.0 ± 6.6	26.2 ± 4.1	27.5 ± 3.0
(breaths	RL	26.7 ± 4.0	22.8 ± 3.6	24.7 ± 6.8	25.3 ± 5.9	23.3 ± 2.3	24.7 ± 4.6	25.3 ± 6.9
/min	LL	23.7 ± 5.6	25.3 ± 2.5	23.3 ± 1.5	26.3 ± 3.9	26.8 ± 4.4	24.5 ± 13.5	28.3 ± 5.6
	SUP	25.3 ± 3.9	26.3 ± 6.9	24.8 ± 6.0	25.0 ± 2.8	28.2 ± 2.2	27.2 ± 6.9	26.7 ± 7.3
	PP	27.0 ± 5.7	27.2 ± 3.7	25.5 ± 3.7	30.8 ± 4.0	27.7 ± 2.7	29.2 ± 2.5	30.3 ± 4.0
	STP	87.0 ±6.1	90.5 ± 4.1	90.3 ± 3.0	89.2 ± 5.9	90.5 ± 4.2	91.3 ± 4.8	91.0 ± 8.8
SPO_2	RL	93.7 ± 1.2	92.7 ± 5.5	92.2 ±3.2	94.5 ± 3.9	91.5 ± 6.4	95.2 ± 3.8	92.3 ± 5.9
(%)	LL	89.7 ± 8.6	93.8 ± 6.2	94.2 ± 5.7	91.7 ±8.8	92.5 ± 2.4	93.2 ± 1.6	92.2 ±2.8
	SUP	91.2 ± 7.6	92.3 ± 5.6	92.7 ± 4.6	94.3 ± 3.9	91.3 ± 5.8	94.0 ± 3.2	93.5 ± 2.7
	PP	93.3 ± 3.4	94.3 ± 3.1	91.3 ± 4.1	92.2 ± 7.4	92.8 ± 5.2	89.8 ± 5.2	91.5 ± 2.0
RT	STP	38.8 ± 0.4	38.7 ± 0.2	38.7 ± 0.3	38.7 ± 0.3	38.6 ± 0.3	38.6 ± 0.4	38.4 ± 0.4
˚C	RL	38.8 ± 0.3	38.4 ±0.3	38.2 ± 0.2	38.2 ± 0.3	38.0 ± 0.3	38.2 ± 0.5	37.9 ± 0.4
	LL	38.0 ± 1.1	37.7 ± 1.2	37.6 ± 1.0	37.5 ± 1.1	37.4 ± 1.0	37.4 ± 0.9	37.2 ± 1.1
	SUP	38.5 ± 0.7	38.3 ± 0.7	38.3 ± 0.7	38.1 ± 0.7	38.2 ± 0.7	38.0 ± 0.7	38.0 ± 0.7
	PP	38.8 ± 0.5	38.7 ± 0.6	38.7 ± 0.5	38.6 ± 0.6	38.6 ± 0.5	38.6 ± 0.5	38.6 ± 0.6

Superscript (*) indicates significant ($p<0.05$) decrease compared with the standingposition

Data are expressed as Mean ± SD of sixgoats

HR: Heart Rate MAP: Mean Arterial Blood Pressure

RR: Respiratory Rate SPO_2: Oxygen SaturationRT: Rectal Temperature

4.3.1 Cardiopulmonary Responses

Figure 4.3.1 compares the mean HR of acepromazine-sedated goats in STP, RL, LL, SUP and PP. Mean HR in only LL was significantly ($p<0.05$) lower compared with values in STP. There were no significant ($p>0.05$) differences in the HR of RL, SUP and PP compared with STP. The MAP in RL, LL and SUP (Figure 4.3.2) were significantly ($p<0.05$) lower compared with the MAP in STP. Mean arterial pressure in PP was not significantly ($p>0.05$) different from STP. There were no significant ($p>0.05$) differences in the respiratory rate (Figure 4.3.3), SPO_2 (Figure 4.3.4) and rectal temperature (Figure 4.3.5) of acepromazine-sedated goat in RL, LL, SUP and PP compared to the STP values.

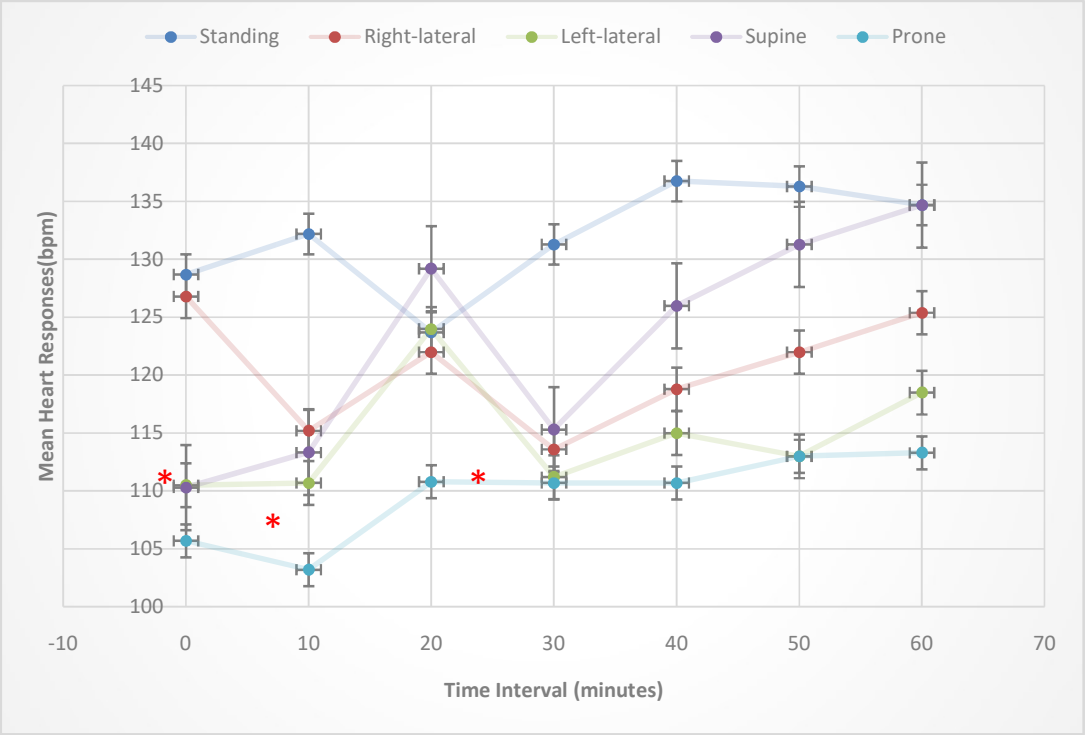

Figure 4.3.1: Comparison of the Mean heart rate responses of acepromazine-sedated goats to STP, RL, LL, SUP andPP

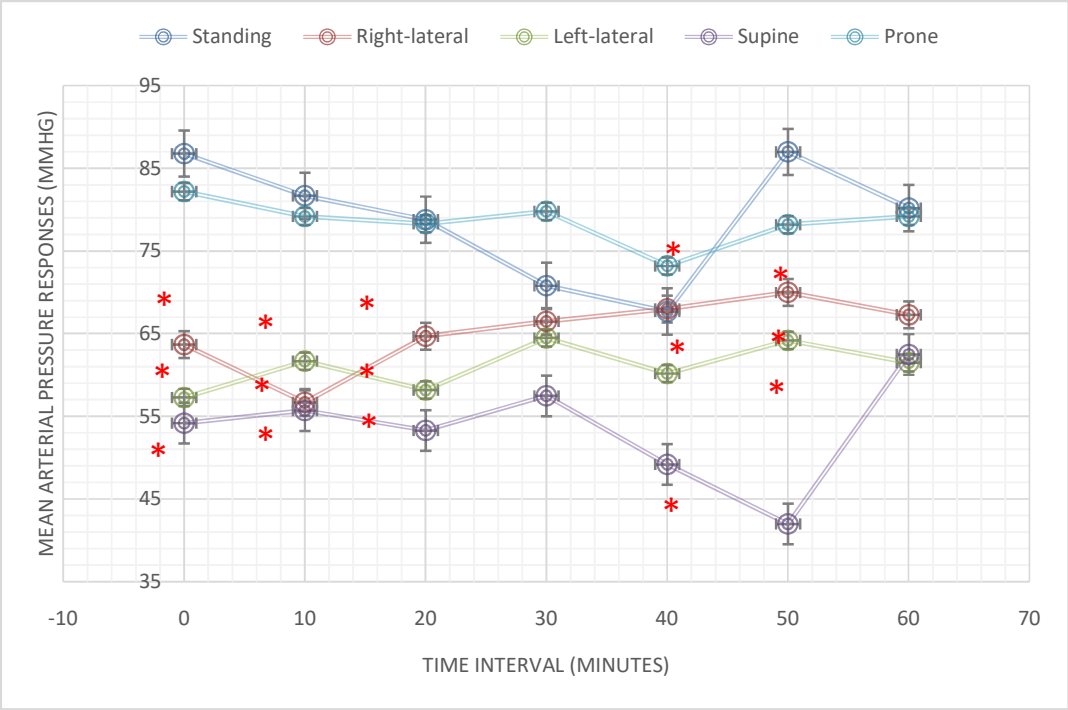

Figure 4.3.2: Comparison of the Mean Arterial Pressure responses of acepromazine-sedated goats to STP, RL, LL, SUP andPP

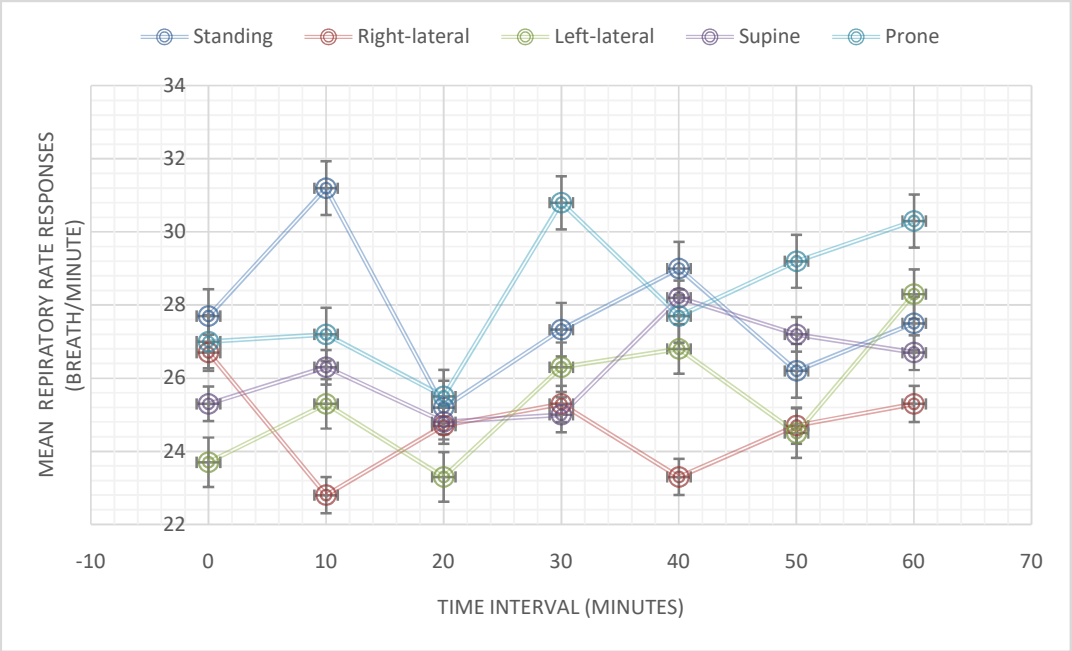

Figure 4.3.3: Comparison of the respiratory rate responses of acepromazine-sedated goats to STP, RL, LL, SUP andPP

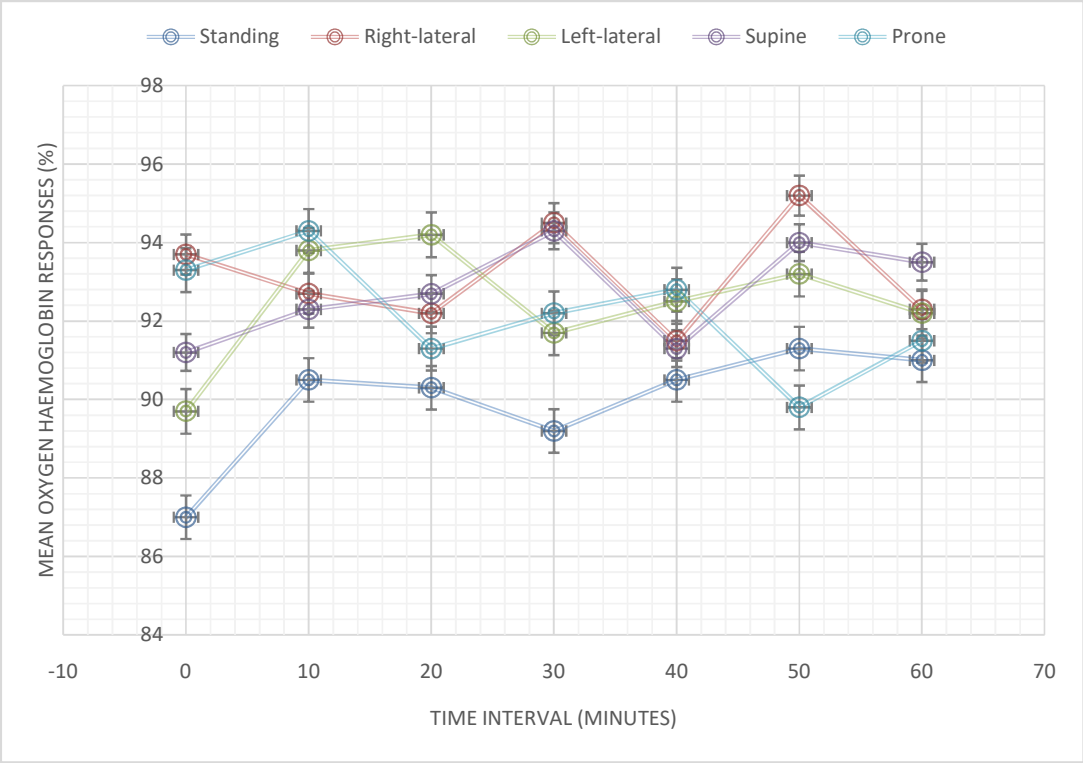

Figure 4.3.4: Comparison of the oxygensaturation responses of acepromazine-sedated goats to STP, RL, LL, SUP and PP

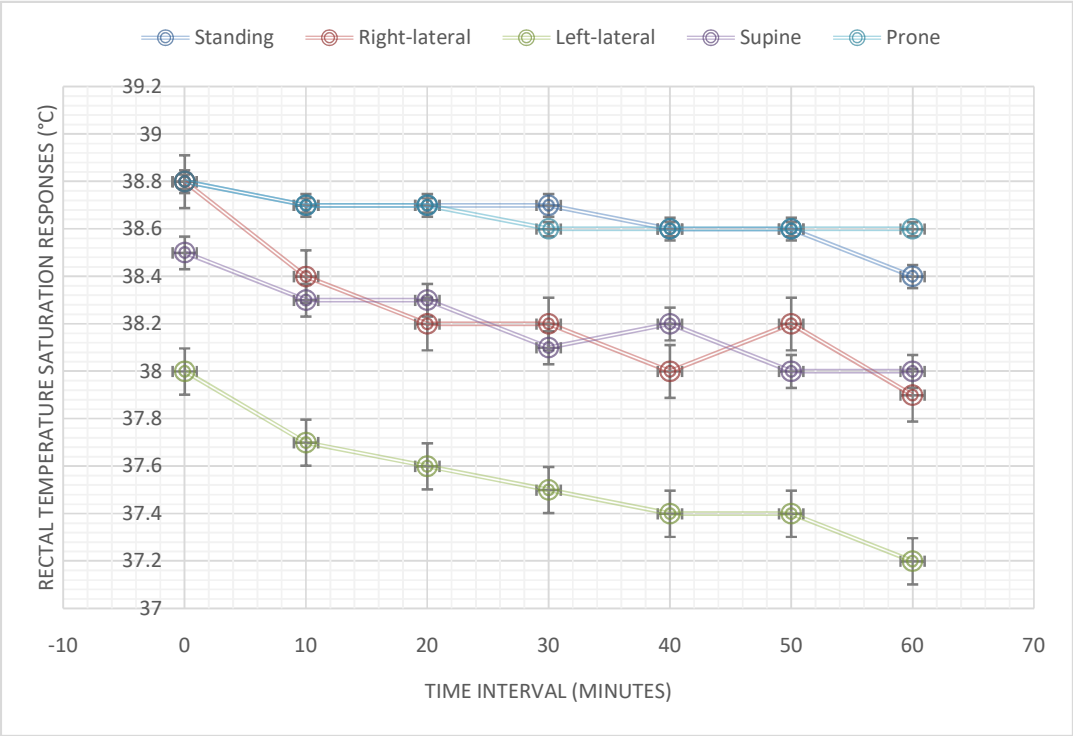

Figure 4.3.5: Comparison of the rectal temperature responses of acepromazine-sedated goats to STP, RL, LL, SUP and PP

4.4 Stress Responses

Plasma cortisol responses of acepromazine-sedated goats to all body positions studied are shown in Figure 4.4.1 Mean plasma cortisol levels at 60min rose above corresponding base line levels for STP, RL, LL, SUP and PP. After 60 minutes, mean plasma cortisol levels were significantly ($p<0.05$) higher in RL, LL, SUP and PP than in STP. Mean blood glucose responses of acepromazine-sedated goats to all body positions are shown in Figure 4.4.2 At 60minutes, mean blood glucose levels rose above corresponding baseline values for STP, LL and SUP while it was lower in RL and PP. Mean blood glucose was significantly ($P<0.05$) higher in LL and SUP compared with standing values while it was significantly ($P<0.05$) lower in RL than in STP. There was no significant ($P>0.05$) difference in PP compared with that of STP. Figure 4.4.3shows the mean plasma LDH of acepromazine-sedated goats to all studies body positions. Mean plasma LDH levels for STP, RL, LL, SUP and PP were lower compared with corresponding baseline values. Only the mean plasma LDH in RL was significantly ($P<0.05$) lower than in STP.

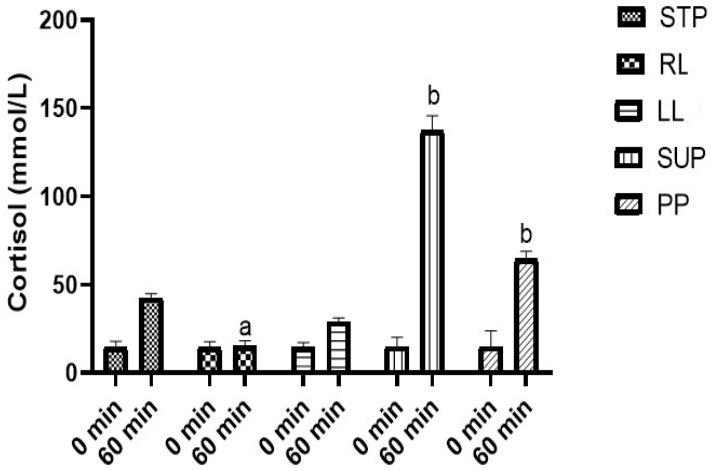

Figure 4.4.1: Cortisol level of acepromazine-sedated goats to body positions. Superscript (a) indicates significant ($p<0.05$) decrease compared with standing position; (b) indicates significant ($p<0.05$) increase compared with standing position. STP = standing position; RL = right lateral position; LL = left lateral position; SUP = supine position; PP = prone position

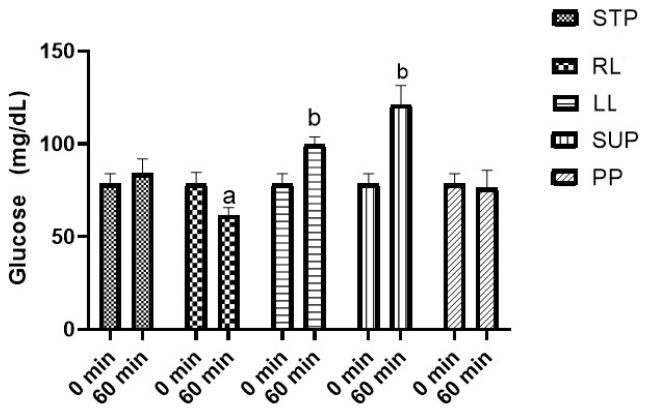

Figure 4.4.2: Glucose level of acepromazine-sedated goats to body positions. Superscript (a) indicates significant ($p<0.05$) decrease compared with standing position; (b)indicates significant ($p<0.05$) increase compared with standing position. STP = standing position; RL = right lateral position; LL = left lateral position; SUP = supine position; PP = prone position

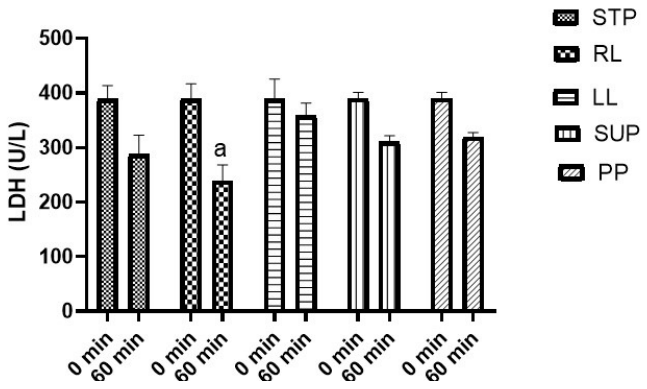

Figure 4.4.3: Lactate dehydrogenase level of acepromazine-sedated goats to body positions. Superscript (a) indicates significant ($p<0.05$) decrease compared with standing position STP = standing position; RL = right lateral position; LL = left lateral position; SUP = supine position; PP = prone position

4.5 Responses of midazolam-sedated goats

4.5.1 Midazolam Sedation

In all the five trials involving midazolam, the sedative agent produced pliable animals that tolerated head and rope restrain. Sedation produced muscle relaxation with no side effect on the goat. No ruminal tympany or salivation was observed. Cardiopulmonary responses of midazolam-sedated goats to STP, RL, LL, SUP and PP are shown in Table 4.5.1.

4.5.1: Responses of midazolam-sedated goats to standing, right lateral, left lateral, supine and prone positions.

Cardiopulmonary responses of midazolam-sedated goats to STP, RL, LL, SUP and PP are shown in Table 4.5.1. The ranges of mean HR in STP were 89.2±26.7 to 108.3±35.9 beat/min, in RL from 101.0±12.5 to 110.3±28.8 beat/min and from 84.2±14.0 to 97.0±12.1 beat/min in LL.The mean HR in SUP ranged from 139.3±20.2 to 150.5±21.9 beat/min, and from 98.3±13.6 to 110.5±23.0 beat/min in PP. MAP in STP ranged from 71.0±8.2 to 82.8±13.1mmHg, from 66.8±29.7 to 74.3±8.2mmHg in RL and from 56.2±12.3 to 69.0±12.5mmHg in LL. MAP in SUP ranged from 65.3±15.1 to 74.2±18.6mmHg and from 89.5±4.5 to 102.3±17.6mmHg in PP. The ranges of RR in STP were from 25.3±3.9 to 29.3±3.8 breath/min, 24.0±3.6 to 26.7±6.8 breath/min in RL and from 21.2±4.0 to 25.3±3.9 in LL.The recorded RR in SUP ranged from 25.3±4.2 to 28.3±6.2 breath/min and from 29.2±5.1 to 33.5±1.1 breath/min in PP. SPO_2 in STP ranged from 88.3±4.7 to 93.7±2.7%, from 90.3±4.9 to 94.0±3.8% in RL and from 89.8±3.8 to 93.5±3.0% in LL. The ranges of SPO_2 in SUP were from 92.3±4.7 to 94.7±3.1% and from 88.0±5.0 to 91.5±5.4% in PP. Mean RT in STP ranged from 38.4±0.2 to 38.8±0.2°C, from 38.0±0.5 to 39.0±0.4°C in RL and from 37.1±0.8 to 37.9±0.5°C in the LL. RT in SUP ranged from 38.0±0.3 to 38.7±0.5°C and from 38.2±0.3 to 38.6±0.5°C in PP.

Table 4.5.1: Cardiopulmonary responses of midazolam sedated goats to STP, RL, LL, SUP and PP

Parameters	Position	Time Interval (minutes)						
		0	**10**	**20**	**30**	**40**	**50**	**60**
	STP	89.2 ± 26.7	107.0 ± 30.4	108.3 ± 35.9	95.3 ± 23.7	93.0 ± 22.3	102.3 ± 25.1	99.0 ± 25.8
HR	RL	101.0 ±21.5**	104.33 ± 25.8	110.3± 28.8	107.3 ± 16.6	108.3 ± 24.3**	106.5 ± 17.2	108.5 ± 18.6
(beats/min)	LL	84.2 ± 14.0	89.7 ± 15.3	93.5 ± 24.0	90.0 ± 21.9	93.7 ± 19.7	90.3 ± 24.0	97.0 ± 22.1
	SUP	139.3 ± 20.2**	140.3 ± 27.3**	145.3 ± 20.7**	142.8 ± 26.9**	150.5 ± 21.9**	144.3 ± 25.9**	146.8 ± 21.3**
	PP	101.3 ± 16.9	99.0 ± 11.7	105.3 ± 19.9	107.7 ± 23.6	98.3 ± 13.6	107.3 ± 15.3	110.5 ± 23.0
	STP	75.0 ± 9.5	82.8 ± 13.1	77.3 ± 12.6	71.0 ± 8.2	75.0 ± 10.9	76.3 ± 7.9	73.8 ± 13.9
MAP	RL	74.3 ± 8.2	71.8 ± 9.3	73.0 ± 8.4	71.2 ± 5.5	69.3 ± 10.7	66.8 ± 29.7	74.2 ± 5.9
(mmHg)	LL	56.2 ±12.3*	68.2 ± 8.8*	63..2 ± 16.9	62.3 ± 19.9	69.0 ± 12.5	68.0 ± 18.9	68.0 ± 10.9
	SUP	65.3 ± 15.1	74.2 ± 18.6	74.1 ± 14.8	73.7 ± 17.9	67.0 ± 13.7	69.7 ± 20.0	67.5 ± 12.1
	PP	102.3 ± 17.6**	96.8 ± 13.4	89.5 ± 4.5	97.7 ± 22.2**	95.8 ± 8.7**	101.7 ± 9.4**	94.8 ± 8.4**
RR	STP	25.3 ± 3.9	25.8 ± 3.6	28.7 ± 5.2	29.3 ± 3.8	28.8 ± 2.5	26.2 ± 2.1	25.8 ± 1.7
(breaths/	RL	24.0 ± 3.6	24.7 ± 4.2	26.3 ± 6.0	24.3 ± 6.3	25.0 ± 3.2	24.7 ± 6.0	26.7 ± 6.8
min	LL	22.0 ± 2.9	22.2 ± 4.8	25.2 ± 5.2	25.3 ± 3.9	21.2 ± 4.0	24.2 ± 4.7	23.3 ± 5.3
	SUP	26.8 ± 2.3	25.7 ± 3.6	25.3 ± 4.2	26.0 ± 4.2	28.3 ± 6.2	28.3 ± 2.0	27.2 ± 3.7
	PP	30.3 ± 4.0	29.2 ± 5.1	31.3 ± 7.8	32.5 ± 2.9	29.3 ± 3.8	33.5 ± 1.1**	30.3 ± 3.8
	STP	93.7 ± 2.7	92.2 ± 4.5	88.8 ± 4.8	88.3 ± 4.7	90.5 ± 7.9	91.3 ± 5.7	93.3 ± 4.1
SPO_2(%)	RL	92.5 ± 2.7	90.3 ± 4.9	93.5 ± 3.3	92.5 ± 2.8	92.0 ± 1.9	93.2 ± 3.6	94.0 ± 3.8
	LL	91.3 ± 3.7	93.5 ± 3.0	91.8 ± 4.5	89.8 ± 3.8	92.5 ± 3.8	92.3 ± 4.4	92.2 ± 5.6
	SUP	92.3 ± 4.7	93.7 ± 2.9	94.7 ± 2.9	94.5 ± 3.7	93.7 ± 3.7	94.0 ± 4.8	94.7 ± 3.1
	PP	91.2 ± 4.6	90.7 ± 4.5	90.2 ± 4.3	88.0 ± 5.0	89.3 ± 3.9	91.5 ± 5.4	91.3 ± 4.9
RT	STP	38.8 ± 0.2	38.7 ± 0.1	38.5 ± 0.1	38.5 ± 0.1	38.4 ± 0.2	38.4 ± 0.2	38.5 ± 0.3
˚C	RL	39.0 ± 0.4	38.3 ± 0.7	38.2 ± 0.7	38.1 ± 0.6	38.0 ± 0.6	38.0 ± 0.6	38.0 ± 0.5
	LL	37.9 ± 0.5	37.7 ± 0.6	37.5 ± 0.7	37.2 ± 0.9	37.1 ± 0.9	37.1 ± 0.8	37.1 ± 0.8
	SUP	38.7 ± 0.5	38.3 ± 0.4	38.2 ± 0.4	38.1 ± 0.3	38.0 ± 0.4	38.0 ± 0.3	38.0 ± 0.3*
	PP	38.6 ± 0.5	38.4 ± 0.4	38.4 ± 0.3	38.2 ± 0.3	38.2 ± 0.3	38.2 ± 0.3	38.2 ± 0.3

Superscript (*) indicates significant ($p<0.05$) decrease compared with the standing position

Superscript (**) indicates significant ($p<0.05$) increase compared with the standing position

Data are expressed as Mean ± SD of sixgoats

MAP: Mean Arterial Blood Pressure

HR: Heart Rate

RT: Rectal Temperature

RR: Respiratory Rate

SPO_2: Oxygen Saturation

4.5.1: Cardiopulmonary Responses

Figure 4.5.1 shows the comparison of mean heart rate of midazolam-sedated goat in STP, RL, LL, SUP and PP. Mean HR was significantly ($P<0.05$) higher in RL and SUP compared to STP. Mean HR in LL and PP were significantly ($P>0.05$) different from STP. The MAP in LL was significantly ($P<0.05$) lower than in STP (Figure 4.5.2) while MAP in PP was significantly ($P<0.05$) higher compared with STP. Mean arterial blood pressure in RL and SUP were not significantly ($P>0.05$) different than in STP. There were no significant ($P>0.05$) differences in respiratory rate(Figure 4.5.3), SPO_2(Figure 4.5.4) and rectal temperature(Figure 4.5.5) in RL, LL, SUP and PP compared to the STP values.

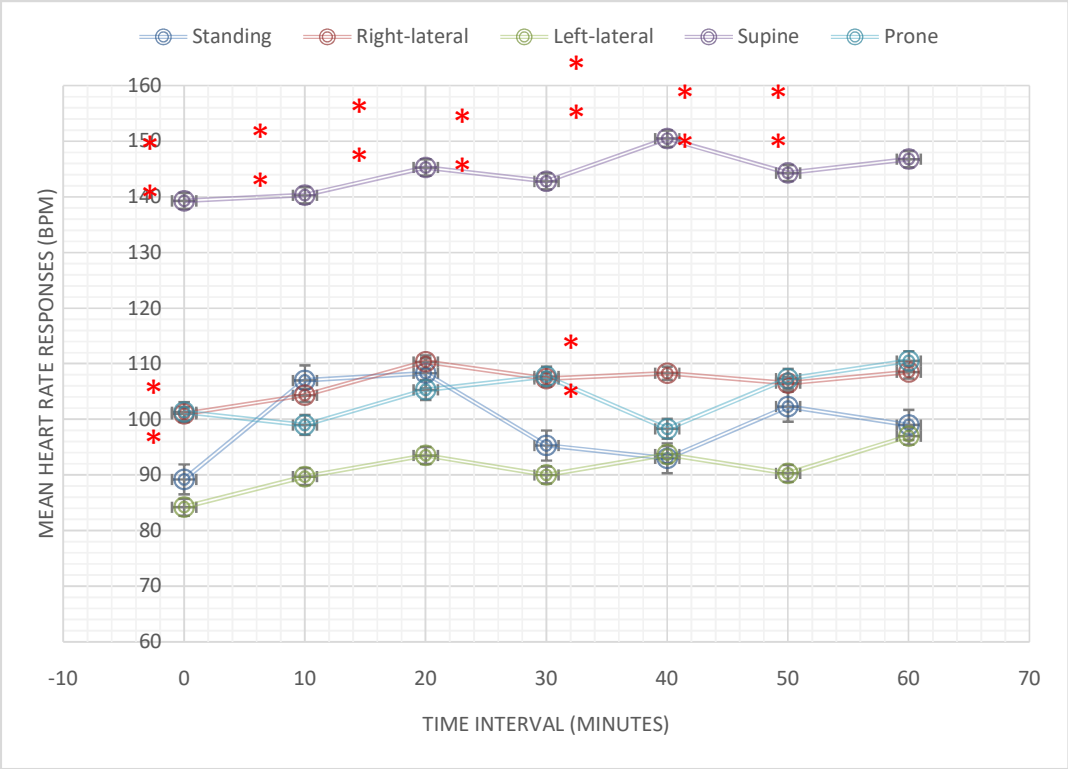

Figure 4.5.1: Comparison of the heart rate responses of midazolam-sedated goats to STP, RL, LL, SUP and PP

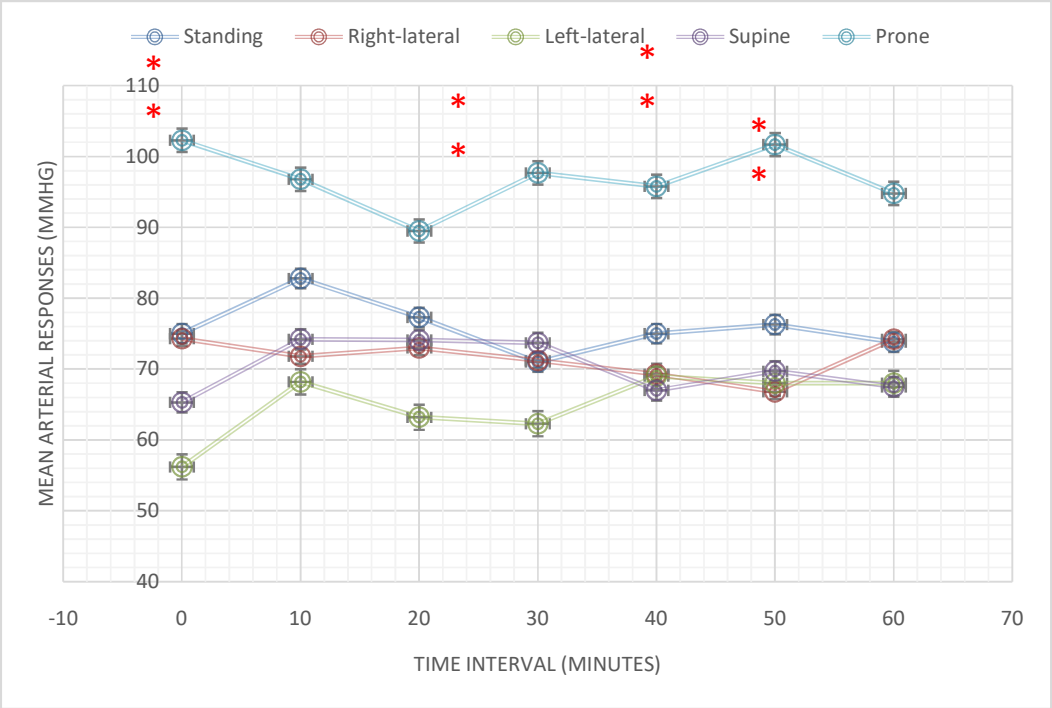

Figure 4.5.2: Comparison of the Mean Arterial Pressure responses of midazolam-sedated goats to STP, RL, LL, SUP and PP

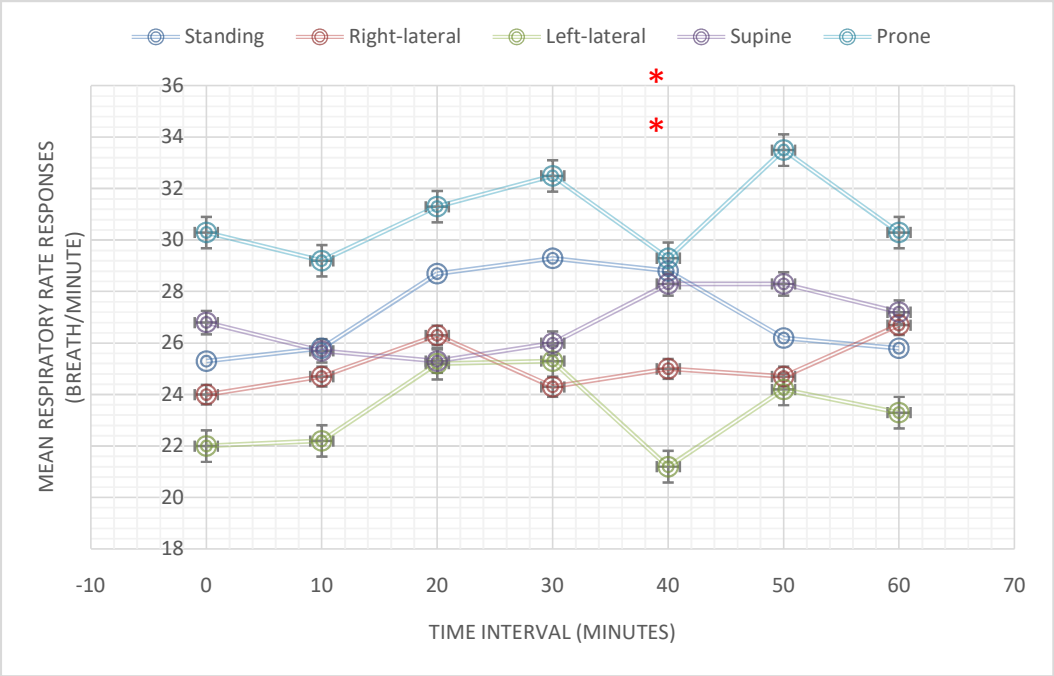

Figure 4.5.3: Comparison of the Respiratory Rate responses of midazolam-sedated goats to STP, RL, LL, SUP and PP

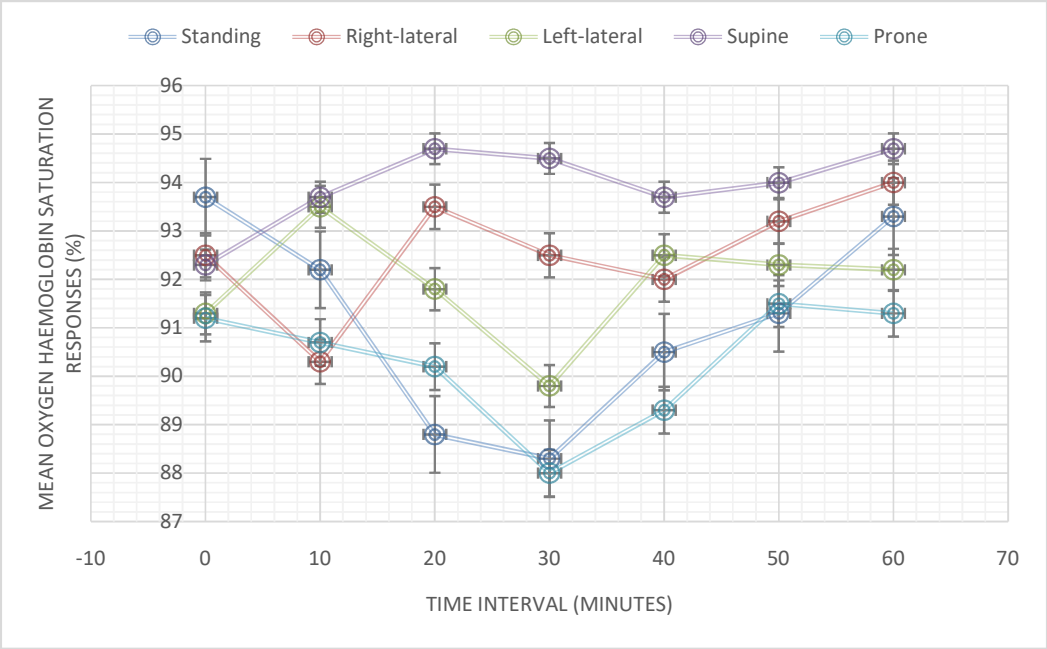

Figure 4.5.4: Comparison of the oxygen haemoglobin saturation responses of midazolam-sedated goats to STP, RL, LL, SUP and PP

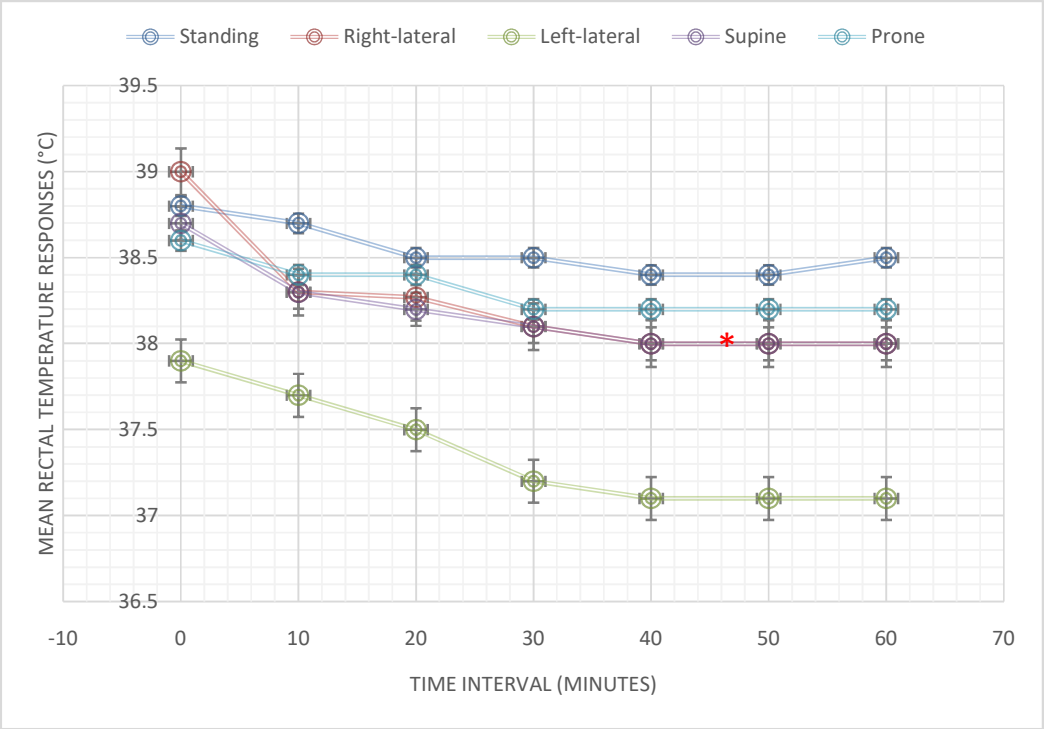

Figure 4.5.5: Comparison of the Rectal Temperature responses of midazolam-sedated goats to STP, RL, LL, SUP and PP

4.6: Stress Responses

Plasma Cortisol responses of midazolam-sedated goats to all the studied body position are shown in Figure 4.6.1. Mean plasma cortisol levels at 60 min rose above corresponding baseline values for STP, LL, SUP and PP while it was lower in RL. After 60minutes, mean plasma cortisol levels were significantly ($P<0.05$) higher in LL and PP than in STP while it was significantly ($P<0.05$) lower in RL than in STP. Mean glucose responses of midazolam-sedated goats to all studied body positions are shown in Figure 4.6.2. At 60minutes, mean blood glucose levels rose above corresponding baseline levels for STP and PP while it was lower in RL, LL and SUP. Mean blood glucose levels in RL was significantly ($P<0.05$) lower than in STP. There were no significant ($P>0.05$) differences in mean blood glucose in LL, SUP and PP compared with STP. Figure 4.6.3 shows the mean plasma LDH of midazolam-sedated goats to all the studied body positions. Mean plasma LDH levels for STP, RL, LL SUP and PP were lower compared to corresponding baseline values. Only mean plasma LDH in LL was significantly ($P<0.05$) higher compared with STP.

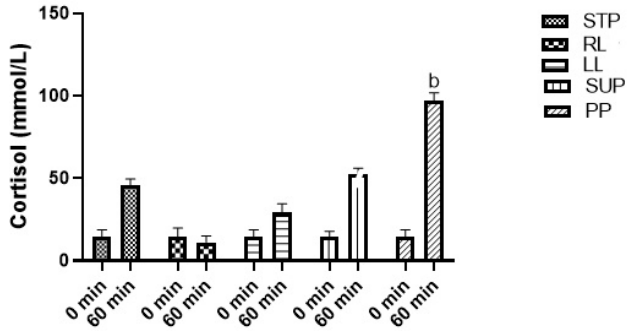

Figure 4.6.1: Cortisollevel of midazolam-sedated goats to body positions. Superscript (b) indicates significant ($p<0.05$) increase compared with standing position. STP = standing position; RL = right lateral position; LL = left lateral position; SUP = supine position; PP = prone position

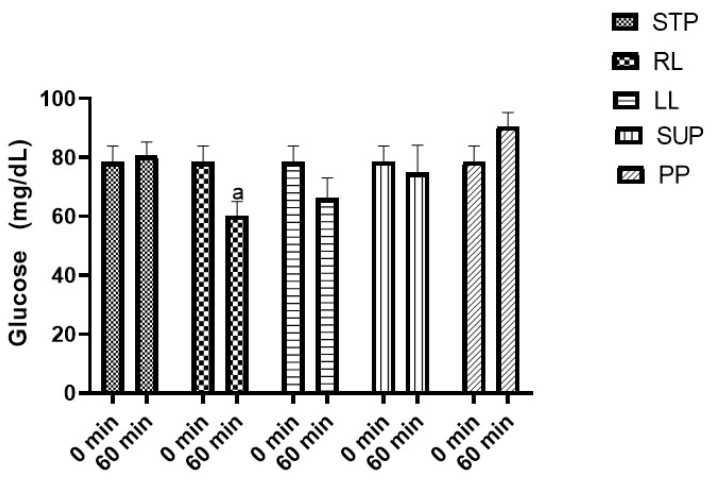

Figure 4.6.2: Glucoselevel of midazolam-sedated goats to body positions. Superscript (a) indicates significant ($p<0.05$) decrease compared with standing position. STP = standing position; RL = right lateral position; LL = left lateral position; SUP = supine position; PP = prone position

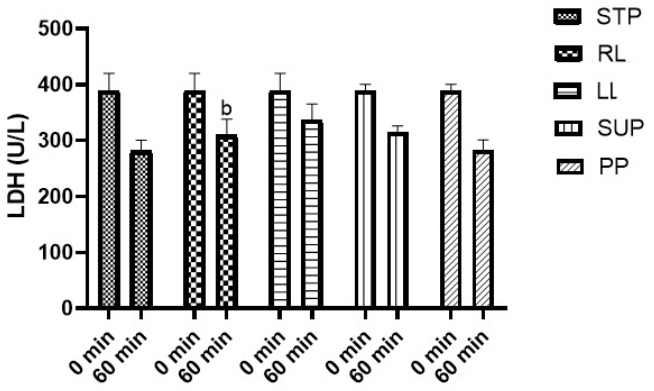

Figure 4.6.3: Lactate dehydrogenaselevel of midazolam-sedated goats to body positions. Superscript (b) indicates significant ($p<0.05$) increase compared with standing position. STP = standing position; RL = right lateral position; LL = left lateral position; SUP = supine position; PP = prone position

CHAPTER FIVE

5.0 DISCUSSION

The experimental goats were sedated in addition to physical restrain in order to make their body positioning somewhat comfortable with minimal movement in line with current clinical practice. The sedative agents employed were chosen on the basis of their local availability and frequent use with caprine practice. Specialized chute was constructed to aid standing position and immobilize the animals' head during the course of the experiment.

Arterial blood pressure can be assessed directly or indirectly in animals. Direct method of blood pressure measurement involves canulation of a suitable peripheral artery with an attached transducer (Haskin, 2005). This invasive method provides accurate blood pressure measurement, facilitates blood gas analysis and blood collected can be used for extended period of time. Indirect method involves the use of inflatable cuffs that are about 40% of the circumference of the appendage which are applied firmly but not tightly over an artery.

In this study, the indirect method was employed because it is quicker, non-invasive, less risky and minimal professional skill is requiredcompared to direct method (Clarke *et al*., 2014). Furthermore, trends rather than absolute blood pressure readings were needed. Normal blood pressure varies throughout the cardiac cycle as the ventricles contract and relaxes. Systolic blood pressure is produced by the contraction of the left ventricle as it propels blood through the systemic arteries. Diastolic blood pressure is the pressure that remains in the arteries when the heart is in its resting phase between contractions. The MAP is the average pressure through the cardiac cycle and is the most important value because it represents actualtissue perfusion of the internal organs. For these reasons, only the MAP was considered in this study. A multiparameter electronic monitor with ability to display data on the screen was employed to facilitate measurement of numerous cardiopulmonary variables at short intervals.

It is usual to take preanaesthetic baseline cardiopulmonary parameters but this was not done in this study for several reasons; first, such preanaesthetic values are easily obtained in companion animals that are used to human handling but difficult in farm animals that will tend to resist handling and instrumentation. Secondly, such physiological parameters are usually quoted in ranges rather than as absolute values. Therefore, it will be difficult to establish such baseline ranges with only six experimental animals. Thirdly, this research makes use of trends rather than absolute values in the physiological parameters.

5.1 Responses of xylazine-sedated goats to STP, RL, LL, SUP and PP

5.1.1 Cardiopulmonary Responses

In the xylazine study, the HR of standing sedated goats ranged from 66 to 78beats/minute, which is on the lower side of normal range of 70-90bpm quoted for awake goat (Muir *et al*., 2013).Excessively slow heart rate allows enough diastolic filling time but the rate cannot maintain cardiac output (Haskin, 2005). This finding of reduced heart rate might be explained by the action of xylazine, an alpha$_2$ adrenoceptor agonist (Pypendop & Verstegen, 1998). Whereas each goat received equal dose of xylazine sedation, mean HR in the RL, LL and SUP were significantly ($p<0.05$) lower than STP (Figure 4.1.1). This finding might be explained by the baroreflex response to recumbency. In the recumbent position, the circulating blood volume could possibly stretch the aortic arch and carotid sinus walls which then send nervous signal to the CNS, exciting the nuclei of vagus and inhibiting sympathetic outflow. The net result is vasodilation, decreased heart contraction and heart rate (Guyton and Hall, 2006).

Also, the MAP of standing sedated goat ranged from 61-69mmHg, which is below the normal range of 80-110mmHg quoted for awake goats (Haskin, 2005). This lower blood pressure correlated with the slow heart rate discussed above. Furthermore, MAP in the RL, LL and SUP were significantly ($p<0.05$) lower than in the STP. This could be explained by baroreceptor response to recumbency causing vasodilation, reduced heart contraction and heart rate (Merin, 1986). Vasodilation causes pulling of blood in large veins leading to reduced venous return, preload, stroke volume and reduced contractility, resulting from centrally-induced sympathetic outflow (Merin, 1986; Guyton and Hall, 2006). In addition, xylazine also causes bradycardia and myocardia depression leading to 50% reduction in cardiac output (Paddleford and Harvey, 1999;

Valverde and Doherty, 2008). Minimum MAP required for adequate tissue perfusion is put at 60mmHg (Haskin, 2015), MAP in RL, LL and SUP were below this value indicating severe hypotension requiring blood volume support. It is however surprising that the goats used for this experiment recovered without any therapeutic intervention. This survival might be explained by the fact that healthy goats have large physiological reserves from which they can draw as the need arises.

The ranges of respiratory rate in STP, RL, LL, SUP and PP were generally above normal range of 16-24breath/minute quoted for the awake goats (Thomas andLerche, 2016). This finding indicates that experimental goats exhibited tachypnoea probably due to xylazine administration (Mohammed *et al*., 1996). Tachypnoea has been recorded in sheep given xylazine (Raptopoulos *et al.,* 1995). The net result is reduced tidal volume with compensatory increased RR to maintain minute volume. Animals with tachypnoea may have low effective alveolar minutes volumes because they are rebreathing dead space gas and therefore may be ventilating very inefficiently. The impact of the increased RR on pulmonary gas exchange cannot be determined in this study because neither a capnograph nor arterial blood gas analysis was performed. Capnography requires endotracheal intubation under general anaesthesia while blood gas analysis requires canulation of a peripheral artery for blood sampling, procedures which were not included in this study protocol.

Generally, SpO_2 in all the body positions ranged from 79-96% which is below the normal range of 95-98% indicating mild to moderate hypoxaemia (Clarke *et al*., 2014). The causes of hypoxaemia include hypoventilation, decrease fractional inspired oxygen, shunting of blood flow and decreased ability of oxygen to diffuse from the lung into the blood stream in animal breathing room air (Thomas and Lerche, 2016). It has been reported that sheep placed in lateral recumbency under xylazine sedation may show reduced arterial oxygen tension despite no injection of sedative or chemical restraint (Mitchel and Williams, 2008). It is alsointeresting to note that healthy experimental goats recovered without oxygen supplementation presumably because of their physiological reserves.

Mean rectal temperature of xylazine sedated goats in STP ranged from 37-38˚C, this is within the normal value of 35 to 39˚C adequate for metabolic activities (Thomas and Lerche, 2016). This means that the animals were able to maintain normothermia under

xylazine sedation in the absence of such risk factors such as clipping of the hair, use of cold scrub solutions, surgical exposure of large body cavity, application of cold lavage solution and administration of cold intravenous fluid.

5.1.2 Stress Responses

Cortisol is generally considered to be a stress hormone because its levels rise during episode of acute stress (Brook and Marshal, 2001). Physical or mental stress increase ACTH secretion, which in turn stimulate the adrenal cortex to secrete cortisol (Nwe *et al*., 1996; Allen *et al.,* 2014). A spike in cortisol level mobilizes necessary resources, such as by tapping into the body's reserve to produce energy and ensureindividuals return to a stable state (Guyton and Hall*,* 2006). In this study, mean plasma cortisol levels for RL, SUP and PP at 60 minute was moreelevated ($p<0.05$) than in thestanding position. This finding suggests that these body positions were more stressful. It is noteworthy that even xylazine sedation could not prevent the stress response, this reportdoes not corroborate the study bySanhouri*et al*., 1992, who attributed decrease in cortisol level as a result of inhibitory action of xylazine during goat transportation. In practice, prolonged stress could lead to increased morbidity of the patient if not mitigated. The experimental goats were able to cope with the degree of stress because of short duration procedure and large physiological reserves. Mean blood glucose levels in the RL was significantly ($p<0.05$) lower than the standing position value while it was elevated in prone position than standing position. This finding suggests that in stressful periods, insulin resistance causes hyperglycaemia and muscle protein breakdown, which are consequences of severe stress response (Carli, 2014). Howeverin this study, the increased blood glucose recorded might have been caused by temporary hyperglycaemic effect of xylazine (Fayed*et al*.,1989)but also blood glucose would appear to be non-specific for stress. Plasma LDH values for RL, LL, SUP and PP were significantly ($p<0.05$) lower than the standing value. This finding does not correlate with that of cortisol and a study conducted in deer where no correlation between cortisol concentration and LDH activity was recorded(Jones and Price, 1992).

5.2 Responses of acepromazine-sedated goats to STP, RL, LL, SUP and PP

5.2.1 Cardiopulmonary Responses

In this study, the HR in STP ranged from 123-136bpm, which is far above the normal range of 70-90bpm quoted for awake goats (Muir *et al*., 2013). This finding of increased HR is probably due to the effect of acepromazine, which is an alpha blocker causing vasodilation with subsequent hypotensionand reflex bradycardia (Taylor, 1991; Alvaides *et al*., 2008). Mean HR in LL only was significantly ($p<0.05$) lower than the standing value in the first 30 minutes. Mean HR in all body positions was generally not significantly different ($p>0.05$) from STP. This finding implies that recumbency drug-induced baroreflex response was overridden by reflex increases in the heart rate (Pequito *et al*., 2012). Excessively fast heart rate can reduce cardiac output by reducing diastolic filling time and stroke volume (Haskin, 2005).

In this study, MAP in the STP ranged from 67-87mmHg which is lower than the normal range of 80-110mmHg accepted for awake goat (Haskin, 2005). This finding implies acepromazine-induced hypotension (Alvaides *et al*., 2008). Except in PP in which MAP was not significantly ($p>0.05$) different from STP, mean arterial pressure in RL, LL and SUP were significantly ($p<0.05$) lower than in the STP. This finding could be the result of combined effect of recumbency-induced baroreflex responses, vasodilation and hypotensive effect of acepromazine and aortocaval compression in the supine position, resulting in reduced venous return and preload. As the end diastolic volume decreases, cardiac muscle fibre length decreases, and stroke volume decreases, resulting in decreased cardiac output and blood pressure in accordance to Frank Sterling law of the heart (Guytonand Hall, 2006). Since the minimum MAP of 60mmHg is required for adequate tissue perfusion (Haskin, 2005), MAP obtained particularly in SUP was generally life threatening. These experimental goats were able to cope with the recorded hypotension possibly because of their large physiological reserves from which they could draw. Certainly, acepromazine-sedated sick goats would require blood volume support to maintain adequate tissue perfusion.

The mean respiratory rate in all body positions were generally higher than the minimum of 16-24breath/minute recorded for the awake goats (Thomas and Lerche, 2016). This finding of tachypnoea is generally considered inefficient ventilation. The

impact of tachypnoea on pulmonary gas exchange was also not known, although the goats recovered without supportive intervention.

Mean SPO_2 values ranged from 87-95, indicating mild to moderate hypoxia. In clinical practice, oxygen supplementation would be required to ensure optimum oxygen delivery to tissue.

The RT in all the studied body positions was within the normal range of 37-38°C accepted for awake goat (Haskin, 2015). This indicates that acepromazine did not interfere with thermoregulation in the CNS.

5.2.2 Stress Responses

Mean plasma cortisol values in both right and left lateral body positions were significantly ($p<0.05$) lower than in the standing position, but in supine and prone body positions cortisol level was significantly ($p<0.05$) higher compared with the standing position suggesting these latter positions were more stressful. It has been documented that cortisol secretion increases in response to any stress in the body (Brook andMarshal, 2001). Mean blood glucose level in RL was significantly lower compared with STP while it was significantly ($p<0.05$) higher in LL and SUP compared with STP. However, this finding does not completely correlate with that of cortisol. Mean plasma LDH value was significantly ($p<0.05$) lower in RL only compared with the standing position. This finding also agrees with the report documented by Jones and Price (1992) in deer.

5.3 Responses of Midazolam-sedated goats to STP, RL, LL, SUP and PP

5.3.1 Cardiopulmonary Responses

In the midazolam sedation study, the HR in STP ranged from 89-108 bpm, which is within and mildly above the normal range of 70-90bpm quoted for awake goats (Muir *et al*., 2013). This finding of mild increase in HR in the STP could be due to the cardiovascular effect of midazolam via its central effect on the vasomotor center(Lemke, 2007; Dzikiti *et al*., 2014). Since all the experimental goats received the same dose of midazolam, this sedative would appear to stimulate the HR to rise above the normal range in the goats. This is interesting considering that midazolam

reportedly has minimal cardiovascular effect (Dzikiti *et al*.,2014). Mean HR in RL and SUP only were significantly ($p<0.05$) higher than the standing value. This finding could be possibly attributed to the action of midazolam, which has beenshown to induce diminished cardiac output and depress baroreflex thus limited ability to compensate for haemodynamic changes associated with hypovolaemia (Marty *et al*., 1986).

Also, the non-invasive methodfor the evaluation of systemic blood pressure has been unequivocally established as a reproducible way of obtaining reliable clinical parameters in healthy and sick goats (SzalúśJordanow *et al*., 2018).The MAP in the STP ranged from 71-82mmHg (Figure 4.3.2), which is slightly below the normal range of 80-110mmHg quoted for awake goat (Haskin, 2005). This finding corroborates the central effect of midazolam on the vasomotor centres by reducing arterial blood pressure due to decrease in systemic vascular resistance (Katzung, 2004). Mean arterial pressure obtained in LL was significantly ($p<0.05$) lower than in standing while it was elevated in prone position. Certainly, recorded MAP fluctuations were not due to midazolam, which has lower cardiovascular effect in the animal breathing room air. However, the reason behind this finding was not clear but the overall MAP was generally above the minimum of 60mmHg which is the minimum level needed for adequate tissue perfusion (Haskin, 2015).

In the STP, RL, LL, SUP and PP, mean RR were above the normal range of 16-24 breath/min accepted for awake goat (Thomas and Lerche, 2010). The cause of the increase respiratory rate was not clear but might be a response from stress as corroborated below by increased serum cortisol levels. Tachypnoea largely results in dead space ventilation, which does not participate in gas exchange and is therefore considered inefficient ventilation.

In all the studied body positions, mean SPO_2 value ranged from 88-94, indicating mild to moderate hypoxia (Clarke *et al*., 2014). In clinical practice, oxygen supplementation would be required to ensure optimum oxygen delivery to tissue.The monitor used to assess oxygen-haemoglobin saturation (SPO2) is well acceptable in veterinary clinical practice, it can also help to detect desaturation prior toevidence of cyanosis (White and Taylor, 2000; Hofmeister *et al*., 2005).

Also, the RT in all the studied body positions was within the normal range of 38-39°C accepted for awake goat (Haskin, 2015). This indicates that midazolam did not interfere with thermoregulation in the CNS.

5.3.2 Stress Responses

Mean plasma cortisol in the prone position only was significantly ($p<0.05$) elevated compared with standing value while it was significantly lower in RL and LL than in STP. The finding of higher cortisol level in the PP might be due to midazolam-induced relaxation of the limb muscle (Ebert *et al*., 2002). This might have put excess weight on the other musculoskeletal structures such as tendon, ligament and joint. These factors were absent in the laterally recumbent goat. This might relate to the animal's body weight been suspended on the rumen or due to other reasons. Mean blood glucose level was significantly ($p<0.05$) lower in RL only compared with STP. This finding does not also completely correlate with that of cortisol. Plasma LDH value in LL only was significantly ($p<0.05$) higher compared with the standing position and this finding does not corroborate the finding recorded in cortisol.

CHAPTER SIX

6.0 CONCLUSION

Body positioning under sedation provoked measurable cardiopulmonary changes and stress responses in healthy goats.Xylazine sedation was associated with slowing of heart rate, whereas sedation with acepromazine and midazolam was associated with increases in the heart rate in any body position. Also, xylazine-sedated goat placed in RL, LL and SUP positions developed severe hypotension that would require blood volume support for adequate tissue perfusion. Goats sedated with acepromazine or midazolam and placed in similar body positions developed only moderate hypotension that could still maintain adequate tissue perfusion. All other measured parameters in all body positions showed no significant changes. Each body position elicited some stress response detectable by increases in plasma cortisol. Inspite of these recorded physiological changes, all the goats withstood the experiment and recovered on their own without support.

6.1 Contribution to knowledge

This research work provides the first evidence that body positioning alone evokes measurable cardiopulmonary changes and stress responses in goats sedated with xylazine, acepromazine or midazolam. The stress responses evoked could not be blocked by sedation. These findings could exacerbate perioperative morbidity or mortality associated with clinical conditions and therapeutic interventions in caprine practice.

Also, this work shows that alpha$_2$ agonists as represented by xylazine could produce life threatening hypotension even in healthy goats placed in lateral or supine positions. Therefore, this finding suggests the need to provide blood volume support for all goats sedated with such agents for successful outcome.

The result of this work also provides evidence that phenothiazines or benzodiazepines are safer sedative agents than xylazine for use in goats. Of all the three biomarkers

employed in this research, only plasma cortisol levels consistently detected stress response in goats just as in other mammals. However, blood glucose and plasma lactate dehydrogenase level proved to be poor biomarkers of stress response in goats.

6.2 Recommendation

Healthy goats as used in this research are known to have large physiological reserve from which to draw as the need arises; such reserves could be very limited in animals with systemic illness. Therefore, it is recommended that a similar prospective clinical study be carried out on goats with co-morbidity presented for therapeutic intervention as basis for developing critical care protocols for such animals.

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RESPONSES OF GOATS SEDATED WITH XYLAZINE TO RIGHT LATERAL SURGICAL POSITIONING

Data Collection Form

Goat No _____ Weight(Kg)_____ Gender _____

Xylazine(mg)_____ Injectate (ml)_____

Sedation: Time _____ Onset of action _____

Pedal withdrawal reflex: Present _____Absent_____

Monitoring

Time	HR	PR	MAP	SPO_2	RR	RT
0						
5						
10						
15						
20						
25						
30						
35						
40						
45						
50						
55						
60						

Sedation Score	**0**	**1**	**2**	**3**

MEASUREMENTS

Plasma cortisol level:

Plasma lactate level:

Blood glucose level

RESPONSES OF GOATS SEDATED WITH XYLAZINE TO LEFT LATERAL SURGICAL POSITIONING

Data Collection Form

Goat No _____ Weight(Kg)_____ Gender _____

Xylazine(mg)_____ Injectate (ml)_____

Sedation: Time _____ Onset of action _____

Pedal withdrawal reflex: Present _____Absent_____

Monitoring

Time	HR	PR	MAP	SPO_2	RR	RT
0						
5						
10						
15						
20						
25						
30						
35						
40						
45						
50						
55						
60						

Sedation Score	**0**	**1**	**2**	**3**

MEASUREMENTS

Plasma cortisol level:

Plasma lactate level:

Blood glucose level:

RESPONSES OF GOATS SEDATED WITH XYLAZINE TO SUPINE SURGICAL POSITIONING

Data Collection Form

Goat No _____ Weight(Kg)_____ Gender _____

Xylazine(mg)_____ Injectate (ml)_____

Sedation: Time _____ Onset of action _____

Pedal withdrawal reflex: Present _____Absent_____

Monitoring

Time	HR	PR	MAP	SPO_2	RR	RT
0						
5						
10						
15						
20						
25						
30						
35						
40						
45						
50						
55						
60						

Sedation Score	**0**	**1**	**2**	**3**

MEASUREMENTS

Plasma cortisol level:

Plasma lactate level:

Blood glucose level:

RESPONSES OF GOATS SEDATED WITH XYLAZINE TO PRONE SURGICAL POSITIONING

Data Collection Form

Goat No _____ Weight(Kg)_____ Gender _____

Xylazine(mg)_____ Injectate (ml)_____

Sedation: Time _____ Onset of action _____

Pedal withdrawal reflex: Present _____Absent_____

Monitoring

Time	HR	PR	MAP	SPO_2	RR	RT
0						
5						
10						
15						
20						
25						
30						
35						
40						
45						
50						
55						
60						

Sedation Score	**0**	**1**	**2**	**3**

MEASUREMENTS

Plasma cortisol level:

Plasma lactate level:

Blood glucose level:

RESPONSES OF GOATS SEDATED WITH XYLAZINE TO STANDING SURGICAL POSITIONING

Data Collection Form

Goat No _____ Weight(Kg)_____ Gender _____

Xylazine(mg)_____ Injectate (ml)_____

Sedation: Time _____ Onset of action _____

Pedal withdrawal reflex: Present _____Absent_____

Monitoring

Time	HR	PR	MAP	SPO_2	RR	RT
0						
5						
10						
15						
20						
25						
30						
35						
40						
45						
50						
55						
60						

Sedation Score	**0**	**1**	**2**	**3**

MEASUREMENTS

Plasma cortisol level:

Plasma lactate level:

Blood glucose level:

RESPONSES OF GOATS SEDATED WITH MIDAZOLAM TO RIGHT LATERAL SURGICAL POSITIONING

Data Collection Form

Goat No _____ Weight(Kg)_____ Gender _____

Midazolam (mg)_____ Injectate (ml)_____

Sedation: Time _____ Onset of action _____

Pedal withdrawal reflex: Present _____Absent_____

Monitoring

Time	HR	PR	MAP	SPO_2	RR	RT
0						
5						
10						
15						
20						
25						
30						
35						
40						
45						
50						
55						
60						

Sedation Score	**0**	**1**	**2**	**3**

MEASUREMENTS

Plasma cortisol level:

Plasma lactate level:

Blood glucose level:

RESPONSES OF GOATS SEDATED WITH MIDAZOLAM TO LEFT LATERAL SURGICAL POSITIONING

Data Collection Form

Goat No _____ Weight(Kg)_____ Gender _____

Midazolam (mg)_____ Injectate (ml)_____

Sedation: Time _____ Onset of action _____

Pedal withdrawal reflex: Present _____Absent_____

Monitoring

Time	HR	PR	MAP	SPO_2	RR	RT
0						
5						
10						
15						
20						
25						
30						
35						
40						
45						
50						
55						
60						

Sedation Score	**0**	**1**	**2**	**3**

MEASUREMENTS

Plasma cortisol level:

Plasma lactate level:

Blood glucose level:

RESPONSES OF GOATS SEDATED WITH MIDAZOLAM TO SUPINE SURGICAL POSITIONING

Data Collection Form

Goat No _____ Weight(Kg)_____ Gender _____

Midazolam (mg)_____ Injectate (ml)_____

Sedation: Time _____ Onset of action _____

Pedal withdrawal reflex: Present _____Absent_____

Monitoring

Time	HR	PR	MAP	SPO_2	RR	RT
0						
5						
10						
15						
20						
25						
30						
35						
40						
45						
50						
55						
60						

Sedation Score	**0**	**1**	**2**	**3**

MEASUREMENTS

Plasma cortisol level:

Plasma lactate level:

Blood glucose level:

RESPONSES OF GOATS SEDATED WITH MIDAZOLAM TO PRONE SURGICAL POSITIONING

Data Collection Form

Goat No _____ Weight(Kg)_____ Gender _____

Midazolam (mg)_____ Injectate (ml)_____

Sedation: Time _____ Onset of action _____

Pedal withdrawal reflex: Present _____Absent_____

Monitoring

Time	HR	PR	MAP	SPO_2	RR	RT
0						
5						
10						
15						
20						
25						
30						
35						
40						
45						
50						
55						
60						

Sedation Score	**0**	**1**	**2**	**3**

MEASUREMENTS

Plasma cortisol level:

Plasma lactate level:

Blood glucose level:

RESPONSES OF GOATS SEDATED WITH MIDAZOLAM TO STANDING SURGICAL POSITIONING

Data Collection Form

Goat No _____ Weight(Kg)_____ Gender _____

Midazolam (mg)_____ Injectate (ml)_____

Sedation: Time _____ Onset of action _____

Pedal withdrawal reflex: Present _____Absent_____

Monitoring

Time	HR	PR	MAP	SPO_2	RR	RT
0						
5						
10						
15						
20						
25						
30						
35						
40						
45						
50						
55						
60						

Sedation Score	**0**	**1**	**2**	**3**

MEASUREMENTS

Plasma cortisol level:

Plasma lactate level:

Blood glucose level:

RESPONSES OF GOATS SEDATED WITH ACEPROMAZINE TO RIGHT LATERAL SURGICAL POSITIONING

Data Collection Form

Goat No _____ Weight(Kg)_____ Gender _____

Acepromazine(mg)_____ Injectate (ml)_____

Sedation: Time _____ Onset of action _____

Pedal withdrawal reflex: Present _____Absent_____

Monitoring

Time	HR	PR	MAP	SPO_2	RR	RT
0						
5						
10						
15						
20						
25						
30						
35						
40						
45						
50						
55						
60						

Sedation Score	**0**	**1**	**2**	**3**

MEASUREMENTS

Plasma cortisol level:

Plasma lactate level:

Blood glucose level:

RESPONSES OF GOATS SEDATED WITH ACEPROMAZINE TO LEFT LATERAL SURGICAL POSITIONING

Data Collection Form

Goat No _____ Weight(Kg)_____ Gender _____

Acepromazine(mg)_____ Injectate (ml)_____

Sedation: Time _____ Onset of action _____

Pedal withdrawal reflex: Present _____Absent_____

Monitoring

Time	HR	PR	MAP	SPO_2	RR	RT
0						
5						
10						
15						
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30						
35						
40						
45						
50						
55						
60						

Sedation Score	**0**	**1**	**2**	**3**

MEASUREMENTS

Plasma cortisol level:

Plasma lactate level:

Blood glucose level:

RESPONSES OF GOATS SEDATED WITH ACEPROMAZINE TO SUPINE SURGICAL POSITIONING

Data Collection Form

Goat No _____ Weight(Kg)_____ Gender _____

Acepromazine(mg)_____ Injectate (ml)_____

Sedation: Time _____ Onset of action _____

Pedal withdrawal reflex: Present _____Absent_____

Monitoring

Time	HR	PR	MAP	SPO_2	RR	RT
0						
5						
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15						
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30						
35						
40						
45						
50						
55						
60						

Sedation Score	**0**	**1**	**2**	**3**

MEASUREMENTS

Plasma cortisol level:

Plasma lactate level:

Blood glucose level:

RESPONSES OF GOATS SEDATED WITH ACEPROMAZINE TO PRONE HEAD-UP SURGICAL POSITIONING

Data Collection Form

Goat No _____ Weight(Kg)_____ Gender _____

Acepromazine(mg)_____ Injectate (ml)_____

Sedation: Time _____ Onset of action _____

Pedal withdrawal reflex: Present _____Absent_____

Monitoring

Time	HR	PR	MAP	SPO_2	RR	RT
0						
5						
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30						
35						
40						
45						
50						
55						
60						

Sedation Score	**0**	**1**	**2**	**3**

MEASUREMENTS

Plasma cortisol level:

Plasma lactate level:

Blood glucose level:

RESPONSES OF GOATS SEDATED WITH ACEPROMAZINE TO STANDING SURGICAL POSITIONING

Data Collection Form

Goat No _____ Weight(Kg)_____ Gender _____

Acepromazine(mg)_____ Injectate (ml)_____

Sedation: Time _____ Onset of action _____

Pedal withdrawal reflex: Present _____Absent_____

Monitoring

Time	HR	PR	MAP	SPO_2	RR	RT
0						
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45						
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55						
60						

Sedation Score	**0**	**1**	**2**	**3**

MEASUREMENTS

Plasma cortisol level:

Plasma lactate level:

Blood glucose level: