MEKELLE UNIVERSITY

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DEPARTMENT OF VETERINARY SURGERY AND ANATOMY

EVALUATION OF ANALGESIC, CLINICO-PHYSIOLOGICAL AND HEMATOLOGICAL EFFECTS OF CAUDAL EPIDURAL LIDOCAINE AND XYLAZINE IN MALE CATLLE CALVES IN MEKLLE, TIGRAY, ETHIOPIA

BY

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(ID No: CVM/pr003/12)

A Thesis Submitted to the College of Veterinary Sciences, Mekelle University, in Partial Fulfillment of the requirements for the Degree of Master of Veterinary Sciences in Veterinary Surgery and Diagnostic Imaging

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Mekelle, Ethiopia

‘DECLARATION`

I declare that this thesis presents the work carried out by myself and does not incorporate without the acknowledgment of any material previously submitted for a degree or diploma in any university; and to the best of my understanding, it does not contain any materials previously published or written by another person except where due reference is made in the text; all substantive contributions by others to the work presented, including jointly authored publications, are clearly acknowledged.

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LIST OF ABBREVIATIONS

ANOVA	Analysis of variance
BMR	Basal metabolic rate
BW	Body weight
EDTA	Ethylene diamine tetra acetic acid
HBC	Hemoglobin concentration
HR	Heart rate
KG	Kilo gram
Mg	Milligram
PCV	Packed cell volume
RR	Respiratory rate
RT	Rectal temperature
SD	Standard deviation
TEC	Total erythrocyte count

ABSTRACT

An experimental study was performed from Juley 2023 to February 2024 to evaluate the anesthetic, clinico-physiological, and hematological effects of lidocaine and xylazine as epidural analgesia in the local breed of male cattle calves. A total of twelve clinically healthy calves aged 7 to 10 months and weighing between 55 and 78 kg were randomly divided into three groups (L, X, and C) comprising four animals each. Group C was assigned as a control, group L and X received 2% lidocaine (0.22mg/kg) and xylazine (0.03mg/kg) respectively. The agents were administered at the caudal epidural space (the first intercoccygeal epidural space /Co1–Co2/). Analgesia was tested using a pin-prick test on the skin of the tail, perineum, anus, and the upper parts of the hind limbs. Epidural anesthesia and analgesia were produced in all-male cattle calves treated with lidocaine and xylazine. The time of onset and duration of anesthesia was recorded. Clinico-physiological parameters were recorded at 0, 10, 20, 30, 60, 90, and 120 minutes, and hematological parameters were also recorded at 0, 30, 60, 90 and 120 minutes. The onset of analgesia was faster in Group L (4.25±0.65 minutes) compared with that of Group X (11.34±1.65 minutes). Epidural administration of xylazine produced a significantly longer duration of analgesia (138.50±1.29 minutes) than that produced by epidural injection lidocaine (68.75±1.71minutes). The heart rate and respiration rate non-significantly change in Groups L and X, whereas rectal temperature decreased significantly in those groups. The hematological parameters decreased in groups treated with lidocaine and xylazine. There were no significant changes in heart rate, respiration rate, rectal temperature, and hematological parameters in Group C. The overall observation on clinico-physiological and hematological parameters showed that both anesthesia and analgesia induced some alterations in their values but, these alterations were found temporary without any clinical significance. Moreover, lidocaine and xylazine were safely used for caudal epidural analgesia taking into account the anesthetic, clinico-physiological and, hematological parameters in male cattle calves. These findings indicate that lidocaine and xylazine are an economical and useful approach for epidural anesthesia.

Key words*:* Epidural anesthesia, Lidocaine, Male cattle calves, Xylazine

CHAPTER I

1. INTRODUCTION

1.1. Background

Anesthesia is one of the miracles of medicine, without which modern surgical techniques would have been impossible. It is first developed to alleviate pain and provide relaxation for surgery. It is employed in animals for a wide variety of operative interventions. The choice of different types of anesthesia, use of anesthetic and analgesic agents, and route of administration of anesthetic agents all are depending on the animals as well as the surgical procedures (Roy *et al*., 2015).

Ruminants are generally not considered good subjects for general anesthesia mainly because of the hazards of regurgitation and inhalation of ruminal contents or saliva into the lungs if the airway is left unprotected (Hall and Clark, 1983). Therefore, surgical interventions under local anesthesia in standing animals are preferred (Skarda and Tranquilli, 2007). Thus, regional anesthesia produced by epidural injections of anesthetic agents is most frequently employed in these species because this technique is simple, cost effective, and no sophisticated equipment is needed (Skarda and Tranquilli, 2007). It has been shown to have fewer cardiopulmonary and other systemic side effects than general anesthesia and is used for providing operative and postoperative analgesia (Grimm, Lamont, Tranquilli, Greene, and Robertson, 2015). Epidural anesthesia is commonly utilized in veterinary medicine to allow diagnostic, obstetrical, and surgical interventions caudal to the umbilicus in the perineal region of large animals (Skarda and Tranquilli, 2007).

Lidocaine is the most commonly used local anesthetic drug in epidural analgesia but has a relatively short duration of action and may require re-administration of the drug to allow completion of the procedure (Day and Skarda, 1991). In addition, local anesthetic agents indiscriminately block motor, sensory, and sympathetic fibers (Day and Skarda, 1991) that cause vasodilation (due mainly to the inhibition of action potentials via sodium channel blocking in vasoconstrictor sympathetic nerves) (Newton *et al.*, 2007), ataxia, hind limb weakness, and occasionally recumbency.

Epidural administration of agents with a greater duration of action may be more appropriate for procedures requiring long-duration analgesia, but the onset of action is slower than lidocaine (Dugdale, 2020). These agents include opioids and alpha-2 adrenergic agonists that selectively block sensory fibers, thereby providing significant analgesia with a decreased likelihood of rear limb dysfunction (Natalini & Robinson, 2000). Xylazine is an alpha-2 adrenergic receptor agonist, (Skadra and, Muir 1996) and it is most commonly used as a sedative agent in ruminants (Bani Ismail, Jawasreh and Al-Majali, 2010). Among all domestic animals, ruminants are the most sensitive to xylazine (Kinjavdekar, Singh Amarpal, Aithal, and Pawde, 2000). The systemic administration of xylazine in ruminants is associated with moderate to severe cardiopulmonary depression such as bradycardia, hypotension, hypoxemia, and tachypnea (Aminkov *et al*., 1999).

In recent years xylazine has been used epidurally to induce perineal analgesia in many species of animals such as horses (LeBlanc and Eberhart, 1990), cattle (Jean, Skarda, Muir and Hoffsis, 1990), dogs (Fani, Mehesare, Pawshe, Khan and Jadhav, 2008), goats (Kinjavdekar, Singh Amarpal, Aithal and Pawde, 2000) and sheep (Aminkov *et al*., 1999). Ataxia and recumbency may occur also following epidural administration of alpha-2 agonists, especially at higher doses, either due to systemic absorption of the drug and/or to local action on motor nerves (Zaugg and Nussbaum, 1990). However, at appropriate doses, xylazine has been reported to be a suitable agent for providing analgesia without excessive ataxia and recumbency (Lee *et al*., 2003) Because of its prolonged duration of action and decreased disruption of the motor function of the hind limbs, alpha-2 agonists is superior to that induced by anesthetic agents commonly used to provide local anesthesia for surgery in standing cattle (Stafford, Mello, Todd, Ward, and Mcmeekan, 2002).

1.2. Statement of the Problem

Administration of general anesthesia to ruminants may involve pulmonary aspiration due to regurgitation of ruminal contents and saliva (Hall *et al*., 2001). In addition, the equipment used to deliver general anesthesia (anesthesia machine supplier) is expensive; it can be difficult to administer anesthesia to cattle in clinical fields, as another person must monitor the anesthesia during use. For this reason, epidural anesthesia such as lidocaine and xylazine are common when performing surgery or examination in ruminants with the animal in the standing position. The process of selecting medications for an anesthetic procedure begins with a review of the patient's history and physical examination.

Additional considerations include knowledge of concurrent medications and possible medication interactions. The anesthesia team to have a working knowledge of anesthetic and analgesic drugs, including advantages, disadvantages, and potential side effects. So there is a lack of documented information regarding the anesthetic, clinico-physiological and hematological effects of lidocaine and xylazine using epidural analgesia in male cattle calves in Ethiopia, Tigray is led to conduct this study. So, this study was designed to assess and evaluate the effects of epidural administration of lidocaine and xylazine on the anesthetic, clinico-physiological, and hematological parameters in male cattle calves.

1.3. Objectives

1.3.1. General objective

- The objective of this study was to evaluate the analgesic, clinico-physiological and hematological effect of lidocaine and xylazine as epidural analgesia in male cattle calves

1.3.2. Specific objectives

- To evaluate the analgesic effect of epidural administration of lidocaine and xylazine as epidural anesthesia in male cattle calves
- To evaluate clinical effect of epidural analgesia lidocaine and xylazine in male cattle calves
- To evaluate hematologic effect of epidural analgesia lidocaine and xylazine in male cattle calves

1.4. Significance of the Study

Epidural analgesia can be provided safely in appropriate patients undergoing major surgery. It offers several proven benefits as a result of pain relief and obtunding the stress response. Epidural analgesia has not been convincingly shown to alter postoperative mortality. However, as part of a multimodal perioperative care program, it has been shown to improve the quality of patient recovery and reduce the incidence of serious complications. In addition, epidural analgesia should provide excellent analgesia; this is a major concern of patients and is demonstrated in all major trials. So that the end goal of this research will be to contribute to the well-being of people or animals; such as veterinarians doing surgery at the field level safely. There are also effective and suitable surgical procedures both for the experts and the animals. Epidural analgesia helps to solve diseases surgically using these anesthetic choices and to solve the adverse effects of general anesthesia. Overall epidural analgesia/anesthesia has improved patient satisfaction and perioperative outcomes.

CHAPTER II

2. LITERATURE REVIEW

2.1. Introduction

Pain in farm animals is still an underestimated issue. As described in the 'five freedoms', framework for animal welfare, freedom from pain is essential. Improper management of pain in cattle can result in stress, distress, decreased feed intake, and decreased daily weight gain. Several cost-benefit analyses have shown that factors such as weight gain and productivity improve when pain is managed appropriately. Overall, pain management is an essential aspect of animal welfare and can have significant benefits for both animals and farmers (Steagall *et al*., 2021).

Why then is analgesia still an issue in food-producing animals? The challenges faced are economic, limited available drugs, and the side effects of general anesthesia. In practice, many farms still choose not to use pain-relieving treatment because of the cost of the drugs and regulatory requirements (Steagall *et al*., 2021). Secondly, when anesthetizing ruminants with systemic drugs, it must be considered that they have a large, functional rumen. The size of the rumen can conflict with ventilation, whilst the content of it can increase the chance of regurgitation and/or aspiration. Anesthesia can also interfere with the activity of the fermentation process. There has to be taken into account the possibility of anesthetic-induced tony or bloat (Greene, 2003). Because of these challenges, appropriate techniques are essential to significantly or physiologically reduce pain during certain procedures. These include local blocks, loco-regional analgesia, and epidural analgesia.

Local blocks are a frequently used technique. It provides analgesia whilst the systemic side effects, described earlier, are limited. The concept is that local anesthesia blocks the transmission of pain by the afferent nerve fibers A-delta and C to the central nervous system. A-alfa, A-beta, and A-gamma fibers are responsible for mostly motor function, nociception, and pressure, while B fibers constitute autonomic innervation of viscera (Kam and Power, 2015). The local anesthetic inhibits the function of sodium channels, preventing nerve depolarization and thus signals transmission.

Epidural anesthesia, caudal epidural in particular, is a commonly used method of analgesia in cattle. It is used during surgery, diagnostic purposes, and for obstetrics (Bigham *et al*., 2009). One notable benefit of epidurals is their limited occurrence of side effects compared to general anesthesia. Also, it is a low-cost method that is relatively easy to perform. The caudal epidural can be carried out with the animal either standing or recumbent and requires no additional equipment. A local anesthetic, alpha-2 agonist, or ketamine can be injected into the epidural space. Depending on the volume of anesthetic used, the regions that can be desensitized are only the caudal sacral nerves or further cranially when larger volumes are used (Ismail, 2016).

2.2. Pain

Pain is a complex phenomenon based on pathophysiological and psychological components that are often difficult to recognize and interpret in animals. Nowadays, more emphasis has been given to the matter of pain in different animals due to increasing awareness of animal welfare. That's why, it became compulsory for veterinarians to identify whether an animal was suffering from pain or not. The symptoms of pain in animals were usually recognized by indirect markers that included behavioral, physiological, and ultimately clinical responses (Landa, 2012). Current approaches to animal welfare have made it easy to manage pain in livestock. Local, regional, and general anesthetic agents in combination with some analgesics had been recommended and administered even to perform minor surgical procedures (George, 2003).

2.3. Anesthetic Drugs

Anesthetic can be defined as any agent that produces a local or general loss of sensation, including pain (Singh, 2015). Anesthesia is defined as reversible processes induced by a drug or drug combination that depresses the activity of nervous tissue peripherally (local and regional anesthesia) or centrally (general anesthesia). Many anesthetic drugs are available to provide this activity (Janycel, 2001). Since pain perception is well-developed in ruminants, anesthesia is mandatory when performing surgery. Local or regional anesthesia is a preferred anesthetic method in ruminants (Thurmon *et al*., 1996).

The commonly used local anesthetic agents include lidocaine, mepivacaine, and bupivacaine. Lidocaine has a relatively rapid onset of action and an intermediate duration of about 1 to 2 hours (Lumb and Jones, 1996). Bupivacaine is a long-acting local analgesic. It is about 4 times more potent than lidocaine and is used most commonly for regional nerve block. Lidocaine is approved for use in epidural anesthesia (Sarker *et al*., 2012). Local anesthetics disrupt ion channel function within the neuron cell membrane preventing the transmission of the neuronal action potential (Hilary and Graham, 2005). Local anesthetic drugs are administered to the areas around the nerves to be blocked, which include skin, subcutaneous tissues, and intrathecal and epidural spaces (Lagan and McLure, 2004).

General anesthesia is not commonly used in ruminants as its administration results in several side effects such as ruminal tympany, regurgitation of reticuloruminal contents, aspiration of material or saliva, hypoventilation, hypotension and fluid, and electrolyte imbalances. Ketamine is an example of an injectable general anesthetic while isoflurane is an inhalant (McKelvey and Hollingshead, 2003). Alpha-2 agonists including xylazine, detomidine, and medetomidine induce sedation and analgesia (Khan *et al*., 2004). The distribution of the drug is influenced by the degree of tissue and plasma protein binding of the drug. The more protein bound the agent, the longer the duration of action as a free drug is more slowly made available for metabolism (Plumb, 2005).

The purpose of anesthesia is to provide reversible unconsciousness, amnesia, analgesia, and immobility with minimal risk to the patient. Pre-anesthetic starvation for 18 to 24 hours (or overnight, 12 to 18 hours) should reduce the likelihood of regurgitation by reducing the volume of rumen content. Starvation for very much longer than this may result in a higher liquid component and make regurgitation more likely. Endotracheal intubation with a cuffed tube should be regarded as essential whenever general anesthesia is induced in ruminants (Polly, 1991). Anesthetic drugs, however, compromise patient homeostasis at unpredictable times and in unpredictable ways (Haskins, 1992).

2.4. Types of anesthetic drugs

2.4.1. General Anesthetics

Drugs used to induce complete loss of consciousness, are intended to block the physiologic and conscious response to any painful or unpleasant stimulus. General anesthetics are of two categories injectable and inhalant. Injectable anesthetics can be used to produce short-term anesthesia for minor diagnostic and surgical procedures, or they can be used for induction of general anesthesia followed by maintenance of inhalation anesthesia for longer procedures (Smith and Sherman, 2009).

Common injectable agents include barbiturates (pentobarbitone, thiopental, thiamylal sodium, methohexitone, etc.) and dissociative (ketamine) (Lyon, 2006). Ketamine is a commonly used general anesthetic agent in veterinary practice that has recently gained greater popularity because of its suitability for use as an analgesic agent to prevent the development of chronic pain when administered at sub-anesthetic doses by continuous infusion (Valverde and Gunkel, 2005). Ketamine should be administered in combination with xylazine or diazepam to induce surgical anesthesia (Lin, 2007). Ketamine can be used for anesthesia in ruminants without fear of convulsions. Muscle relaxation is poor, but is improved by sedatives such as diazepam or xylazine (Grant and Upton, 2001).

Common inhalation agents include isoflurane, sevoflurane, and nitrous oxide. From these isoflurane provides a very rapid and smooth induction and recovery may cause some slight respiratory depression. It undergoes very little biotransformation and is almost eliminated in exhaled air. It can only be used in a vaporizer (with or without an induction chamber). It provides no post-operative analgesia (Swindle *et al*., 2002).

2.4.2. Local Anesthetics

Local anesthetics are drugs, which reversibly prevent transmission of the nerve impulse in the region to which they are applied, without affecting consciousness. Local anesthesia induces loss of sensation by reversibly blocking the transmission of nerve impulses along the nerves in a small part of the body that is to be operated on (Lauretti, 2014). Local and regional anesthesias are commonly used in farm animals, as they are considered both safe and effective. Local anesthetics generally have a lipid-soluble hydrophobic aromatic group and a charged, hydrophilic amide group. The bond between these two groups determines the class of the drug and maybe amide or ester. Examples of amides include lidocaine, bupivacaine, and procaine. Examples of esters include cocaine and procaine (Hilary and Graham, 2005).

Anesthesia like paravertebral or epidural nerve block is preferred for most abdominal surgeries in cattle because of side effects from general anesthesia and recumbency. Dorsolumbar epidural anesthesia is produced by the administration of local anesthetic like lidocaine more commonly (Bigham *et al*., 2010)

2.4.3. Regional Anesthetics

This term is used where specific nerves to the area concerned are blocked. Examples include specific nerve blocks to the limbs; paravertebral blocks; corneal blocks (for dehorning) and many others. Paravertebral anesthesia refers to the perineal injection of local anesthesia into the spinal nerves as they emerge from the vertebral canal through the intervertebral foramina (Stafford *et al*., 2002). Local anesthetic drugs, such as lidocaine, are used to block painful sensations in certain parts of the animal body. The anesthesia (or loss of sensation) is often accompanied by a lack of motor control or relaxation of the muscles. Regional nerve block analgesia is of obvious advantage in ruminants and various methods are available (Stafford *et al*., 2002).

2.5. Practical use of epidural anesthesia in ruminants

In veterinary practice for the treatment of different surgical and obstetrical interventions of pelvic region, reproductive, renal system, and hind quarters of domestic animals epidural anesthesia is commonly used (Dehkordi *et al*., 2012). General anesthesia may produce undesirable results in ruminants (Habibian *et al*., 2011), because during general anesthesia animals may take food particles, saliva, or other material into the respiratory tract due to its regurgitating ability (Azari *et al*., 2014).

However, in ruminants, epidural anesthesia is a comparatively uncomplicated method for diagnostic procedures and regional surgery (Khajuria *et al*., 2014). Such as hysterotomy, celiotomy, rumenotomy, repairs of prolapse (vagina, rectum, and uterus) hernia and other abdominal affections, and surgery of the prepuce, penis, or hind limbs (Skarda and Tranquilli, 2007). This type of anesthesia is comparatively safe. Therefore, it is used frequently before to diagnostic, obstetrical, and surgical procedures in ruminants (Khajuria *et al*., 2014). These drugs are cheap, easily available, and have good analgesia (Hall *et al*., 2001). Dissimilar to local infiltration, epidural anesthesia desensitizes all the layers of the abdomen including the peritoneum, and also increases intra-abdominal space in laparoscopy procedures for easy manipulations (Khajuria *et al*., 2014).

Dystocia and prolapse of the uterus are significant problems and have been encountered in ruminants (Bigham *et al*., 2009). Whereas, both conditions could be solved by surgical manipulation (Ismail, 2016). Therefore, anesthesia plays an important role in controlling the animal by using safe anesthetic agents. Meanwhile, ruminants are at high risk for anesthesia, due to several anesthetic complications that have been observed during surgery such as tympany, regurgitation, and muscular structure damage (Habibian *et al*., 2011). Therefore, alternate methods such as; epidural anesthesia is preferred in ruminants to perform many different surgical procedures. Though, dystocia, prolapse of the rectum, prolapse of the uterus, and posterior udder surgery in female animals, problems would be easier to solve when using epidural anesthesia. But epidural anesthesia is also best for castration in buck through surgical methods (Ismail, 2016). However, epidural anesthesia is used in ruminants for the treatment of other obstetrical and surgical interventions of the hind limb area such as; surgery of the anus, vulva, perineum, caudal udder, and scrotum (Ismail, 2016).

2.5.1. Commonly used drugs in epidural anesthesia

The bupivacaine, lidocaine, tramadol, and xylazine are more frequently used drugs for the induction of high epidural anesthesia in ruminants (Ismail, 2016).

Lidocaine

Lidocaine hydrochloride 2% is the local analgesic drug composed of the amino-amide class, which is most commonly used for epidural analgesia in cattle, camel, buffalo, sheep, and goats (Ismail, 2016). This analgesic alters the fast voltage-gated by blocking signal conduction in the sodium channel of the neuronal cell membrane (Skarda and Tranquilli, 2007). In ruminants, lidocaine hydrochloride 2-5 mg/ kg body weight is administered epidurally whereas, the epidural dose rate of lidocaine is different in different animals as mentioned in Table 1. However, it is used with or without other anesthetic agents to produce good analgesia at the tail, anus, and perineum in ruminants (Ismail, 2016). The time of analgesia may be prolonged when lidocaine is mixed with epinephrine (Rostami and Vesal, 2012).

The time of onset of analgesia with lidocaine as epidural anesthesia is 3-5 minutes after administration and the effect remains for 2.5 hours depending on the dose. Usually 2-5 mg/kg body weight is recommended. While, lidocaine produces rapid onset but its effect lasts earlier than xylazine in horses, ponies, and cattle (Ismail, 2016). Furthermore, analgesia produced by lidocaine is relatively short duration, and incremental dose will allow the completion of the surgical procedure (Atiba *et al*., 2015). In addition, local anesthetic agents indiscriminately block motor, sensory, and sympathetic fibers causing ataxia, hind limb weakness, and occasionally recumbency (Ismail, 2016). Lidocaine blocks the sensory, motor, and sympathetic nerves by axonal depression of nerves (DeRossi *et al*., 2005). The drugs with greater duration of action are injected in epidural space for those surgical procedures that require long-duration analgesia (Molaei *et al*., 2010). While sympathetic blockade due to epidural injection of local anesthetics may result in vasodilatation. However, vasodilatation reduces the period of anesthesia and produces hypotension (DeRossi *et al*., 2005).

Xylazine

Xylazine, one of the alpha-2 agonists, has been widely used in veterinary practice both systemically as a sedative and analgesic drug and neuraxial for analgesia in various species (Grubb *et al*., 2002). It causes muscle relaxation and, depending on the dose used, it can induce cardiorespiratory depression, a fall in body temperature, a reduction in ruminal activity, a reduction in swallowing (hence, drooling of saliva) with an increased risk of aspiration, and diuresis (Picavet *et al*., 2004; Zuagg and Nussbaum, 1990).

The use of alpha-2 adrenergic agonists in domestic animals has become famous for good analgesia (Kalhoro, 2006). However, it is more frequently used in veterinary science by noxious stimuli produces analgesia by inhibiting the spinal substance release and nociceptive neuron firing produced by noxious stimuli and produces analgesia and also stimulates the alpha-2 adrenergic receptors of the spinal cord for sedation (Ismail, 2016). However, it causes sedation, hypotension, bradycardia, and respiratory depression in goats and horses (Molaei *et al*., 2010; Kalhoro 2006). These drugs are more effective for epidural or subarachnoid analgesia in domestic animals (Ismail, 2016). The alpha-2 agonists are superior to anesthetic agents because they produce the duration of action and reduce disruption of the motor function of the hind limbs in cattle (Molaei *et al*., 2010).

Xylazine is used for epidural anesthesia in sheep, goats, cows, buffalos, horses, and camels (Singh *et al*., 2005). While epidurally administered alpha-2 agonists produce analgesia by activating presynaptic alpha-2 adrenergic receptors located on primary afferent fibers terminating in the dorsal horn of the spinal cord, as well as postsynaptic alpha-2 receptors located on wide dynamic range projection neurons in the dorsal horn (Schug *et al*., 2006).

Xylazine is used at 0.025 mg/kg to 0.5 mg/kg body weight in ruminants (Ismail, 2016) whereas; the dose rate of xylazine is different in different animals as mentioned in Table 1. When the lowest possible dose of xylazine and lidocaine is used in epidural space, the onset of epidural anesthesia commonly occurs within 10 minutes and the duration of sedation remains for 3-4 hours. Time may be increased up to 5 minutes and 6 hours when xylazine is given at a dose rate of 0.03-0.05 mg/kg body weight and also combined with lidocaine (Ismail, 2016). Meanwhile, the onset of action of xylazine is delayed, but the duration of action is longer by epidural anesthesia in many animal species (Ismail, 2016).

Xylazine induces a state of drowsiness with a high dose-dependent degree of analgesia, generalized muscle relaxation of central origin, and cardiopulmonary depression. Xylazine can even have local anesthetic effects (Derossi *et al*., 2003). Xylazine may produce sedation with a high dose-dependent degree of analgesia, generalized muscle relaxation of central origin, and cardiovascular and respiratory depression when administered parentally into domesticated animals (Molaei *et al*., 2010). It produces analgesia in the perineal region without adverse effects such as hypotension, neuro-toxicities, and severe ataxia of other locally administered anesthetics, when used epidurally in rams, ponies, cattle, horses, and llamas. While, the cardio-pulmonary effect of xylazine is very less when an epidural route is used as compared to the intramuscular route (DeRossi *et al*., 2003).

Presently xylazine is frequently administered into the epidural space in many domestic animals but is contraindicated in cardiovascular patients because it may cause bradycardia, hypotension, and vomiting (Molaei *et al*., 2010).

Table 1: Epidural administration dose rate of xylazine and lidocaine in different animals

Name of animal	Lidocaine	Xylazine
Dog	3-6 mg (Garcia, 2018)	0.75 mg (Fani *et al*., 2008)
Cattle	0.22 mg (Ismail *et al*, 2018	0.05 mg (Grubb *et al*., 2002)
Buffalo	2.0 mg (Singh *et al*., 2005)	0.05 mg (Singh *et al*., 2005)
Goat	2.5 mg (DeRossi *et al*., 2005)	0.1 mg (DeRossi *et al*., 2005)
Rabbit	4 mg (Marjani *et al*., 2014)	3 mg (Marjani *et al*., 2014)

CHAPTER III

3. MATERIALS AND METHOD

3.1. Study Area

The study was carried out in Mekelle, Tigray, Ethiopia. Mekelle is the capital city of the Tigray region in northern Ethiopia. It is located approximately 780 kilometers far away from Addis Ababa in the northern direction and latitudinally located at about $13^0$32' N, longitudinally $39^0$33’ E, and its estimated population are 215,546. Its average elevation above sea level is 2200 meters, and its monthly minimum and maximum temperatures are 8.7 and 26.8 degrees Celsius, respectively. Ecologically the area lies in a dryland ecosystem and the area receives a mean annual rainfall of about 600 millimeters of rain a year on average, with July and August accounting for more than 70% of that total. The extended dry season lasts from October to May (CSA, 2011).

3.2. Study animals

The study was conducted on a total of twelve healthy local breed male cattle calves aged 7–10 months and weighing 55–78 kg, were selected. All calves were declared healthy based on medical history and physiologically normal parameters examination such as rectal temperature, heart rate, respiratory rate, lung sound, mucous membranes, and ruminal movement.

3.3. Study Design and Procedure

An experimental study design was carried out from July 2023 to February 2024 in Meklle to find the effects of lidocaine and xylazine anesthesia on some physiological, hematological, and analgesic indices in male cattle calves. Animal owners were aware of the procedure that was going to be undertaken. A total of twelve clinically healthy male cattle calves (7-10 months’ years old and weighing between 55 and 78 kg) were selected and used in this study. The animals were assigned to three equal groups using randomized block design. Group L (with lidocaine 0.22 mg/kg) and Group X (with xylazine 0.03 mg/kg) were assigned to be injected epidurally and the remaining Group C was a control group. Each animal was kept off feed for 16 hours, and water was withheld for 12 hours before the start of the experiment.

The animals were restrained in a standing position in the crush and the area between the last sacrum and the third intercoccygeal joint was aseptically prepared by clipping the hairs and with surgical scrubbing using povidone-iodine. An 18 G, 3.7 cm length, sterile hypodermic needle was inserted into the epidural space (between coccygeal Co1 and Co2) with the bevel point forward. Proper placement of the needle was determined by the loss of resistance and ease of injection of drugs. After ascertaining the proper positioning of the needle the drugs were administered slowly, approximately over 30 seconds.

In all the animal groups, the time for onset of analgesia and duration of analgesia were recorded. In this study, analgesia was tested in the tail, anus, perineum, and upper hind limb area using a pin-prick method to determine the extent of complete analgesia following epidural administration of the drugs. Time to the onset of analgesia was defined as a time interval (in minutes) from the epidural injection of the drug to loss of response to pin-prick in the perineal region. The duration time of analgesia was defined as a time interval (in minutes) from loss of response up to reappearance of pain response to pin-prick in the perineal region.

The physiological parameters including rectal temperature; respiratory rate and heart rate of the animal were measured before, during, and after recovery from analgesia. Heart rate (HR) was measured by counting the heartbeats over the cardiac area (over the left side of the chest) using a stethoscope. The heartbeats were counted for 15 seconds, multiplied by four, and the result was recorded. Respiratory rate (RR) was measured by observation and counting the abdominal movements. Expiration and inspiration movements were counted as one cycle then respiratory rate was counted for half a minute multiplied by two, and rectal temperature (°C) was measured with a digital thermometer (produce sound after manipulation for about 2 minutes in the rectum).

Blood samples were collected from the jugular vein for hematological parameters before (0 minutes), at 30, 60, 90, and 120-minute intervals after administration of drugs. For hematology, 3 ml venous blood was collected in test tubes containing EDTA.

Hematological parameters including hemoglobin concentration (HBC), packed cell volume (PCV %), and total erythrocytes count (TEC) were examined. Hemoglobin was estimated by Sahli's hemoglobin meter as per the standard method recommended by (Orpet and Welsh, 2001). The values were expressed in g/dL. Packed cell volume was estimated by micro-hematocrit as described by (Feldman *et al.,* 2000), and the values were expressed in percentage. The total erythrocyte count was estimated as per the procedure described by (Orpet and Welsh, 2001) using Neuberger's slide and the values were expressed in million cells per microliter of blood.

3.4. Data Collection

The data were collected on anesthetic effects (onset and duration of anesthesia), physiological parameters (heart rate, respiratory rate, and rectal temperature), and hematological effects (packed cell volume, total erythrocytes count, and hemoglobin concentration).

3.5. Statistical Analysis

All the data collected during the study period was checked, coded, and entered into a Microsoft Excel worksheet and analyzed using STATA version 16. Normality assumptions were checked using histogram and found that all continuous variables were normally distributed. Descriptive statistics was employed to summarize the data and expressed in terms of Mean + Standard deviation. Parametric variables were analyzed statistically using an independent t-test to compare the effect of different treatments at each of the assessment times. One-way ANOVA and Bonferroni tests were utilized for the comparison of mean values for HR, RR, RT, HBC, PCV, TEC induction time, and duration of anesthesia between the treatment groups. For all analysis, a P-value < 0.05 was used as the cutoff value for the significance difference.

3.6. Ethical Consideration

All procedures conducted in this study were carried out according to the College of Veterinary Sciences' Animal Ethics and Experimentation Committee granted ethical approval, and the experiment took into account the Guidelines on Care and Use of Animals for Scientific Purposes.

CHAPTER IV

4. RESULTS

4.1. Anesthetic Effects of Lidocaine and Xylazine

The statistical analysis showed significant differences ($P < 0.05$) among the treatment groups for induction time and duration of anesthesia (table 2). All the animals achieved satisfactory pain relief after epidural injection with lidocaine and xylazine. None of the calves attempted to lie down during any of the treatments. However, one calf in Group X lay down temporarily and salivated moderately which was completely absent at the end of observation.

The time to onset of analgesia and duration of analgesia are presented in Table 2. The onset of analgesia in Group L (4.25±0.65minutes) was significantly ($P < 0.05$) shorter as compared to animals of Group X (11.34±1.65 minutes) (table 2).

Duration of analgesia measured from desensitization of the site after injection and until the animal fully recovered and became responsive to needle prickle. Xylazine produced significantly ($P < 0.05$) longer duration of analgesia (138.50±1.29 minutes) than that produced by lidocaine (68.75±1.71 minutes) (table 2).

Table 2: Anesthetic indices of epidural administered lidocaine and xylazine in male cattle calves (mean ± SD)

Indices	Lidocaine (min)	xylazine (min)
Onset of analgesia	4.25±0.65	11.34±1.65
Duration of analgesia	68.75±1.71	138.50±1.29

4.2. Effects on Physiological Parameters

The mean (± SD) value of heart rates (beats/Min), respiratory rates (breaths/Min), and rectal temperatures (°C) for all of the animals before the epidural injection and at intervals thereafter are given in (table 3, table 4 and table 5)

The effect of lidocaine was associated with a significant (P < 0.05) decrease in RT at 10-60 min (table 3), this was also observed in calves who received xylazine at 10-60 min (table 4). No significant (P > 0.05) change in RT was noticed in Group C (table 5). Other parameters (HR and RR) recorded no significant (P > 0.05) changes at all-time points in all treatment groups.

Table 3: Effects of lidocaine on heart rate, respiratory rate and rectal temperature

	Group L		
Time (min)	**HR (beats/min)**	**RR (breaths/min)**	**RT (C)**
0	68.00±0.82	19.25±0.96	38.05±0.24
10	67.00±0.82	20.25±1.50	37.80±0.29
20	66.75±0.50	20.75±0.96	37.65±0.19
30	66.25±0.96	19.75±0.50	37.55±0.13
60	66.50±0.58	21.00±1.41	37.63±0.10
90	66.75±0.50	20.00±0.82	37.70±0.14
120	67.00±0.82	20.75±1.50	37.76±0.10

HR= Heart rate; RR= Respiratory rate; RT= Rectal temperature

Table 4: Effects of xylazine on heart rate, respiratory rate and rectal temperature

	Group X		
Time (min)	**HR (beats/min)**	**RR (breaths/min)**	**RT (C)**
0	67.00±0.82	24.00±0.82	38.18±0.39
10	65.75±0.50	24.25±0.50	37.86±0.33
20	66.00±1.44	24.00±0.82	37.48±0.19
30	65.50±0.58	24.00±1.41	37.13±0.10
60	65.75±0.50	23.25±0.50	36.98±0.13
90	66.25±1.71	23.50±1.00	37.26±0.17
120	66.50±1.00	23.50±0.56	37.60±0.22

HR= Heart rate; RR= Respiratory rate; RT= Rectal temperature

Table 5: Evaluation of physiological parameters (HR, RR and RT) on the control group

	Group C		
Time (min)	HR (beats/min)	RR (breaths/min)	RT (C)
0	69.00±1.63	23.00±1.63	38.20±0.22
10	69.00±2.16	23.00±2.16	38.26±0.21
20	68.25±1.50	22.75±1.71	38.23±0.24
30	69.25±1.23	22.50±1.29	38.23±0.24
60	68.50±1.73	23.00±1.63	38.23±0.22
90	69.25±1.50	23.25±1.50	38.25±0.21
120	69.00±1.63	22.75±1.71	38.25±0.19

HR= Heart rate; RR= Respiratory rate; RT= Rectal temperature

4.3. Effects on Hematological Parameters

The hematological variables are shown in Table 6. Although there was no significant ($P > 0.05$) difference in HBC, the mean PCV and TEC decreased significantly ($P < 0.05$) following lidocaine administration (table 6).

The mean PCV also decreased non-significantly ($P > 0.05$) from base value up to 90 min but mean HBC and TEC decreased significantly ($P < 0.05$) at 30 to 90 min after xylazine administration. However, all those parameters increased gradually and returned to baseline level at 90 to 120 min in both groups (table 6).

Hemoglobin, PCV, and TEC remained within the normal range (no significant change ($P > 0.05$) throughout observation in Group C (table 6).

Table 6: Hematological observations before and after epidural administration of lidocaine (group L) or xylazine (group X) and the control group (group C) in male cattle calves

Parameters	Groups	Time interval				
		0 min	**30 min**	**60 min**	**90 min**	**120 min**
HBC (gm/dl)	C	9.48±0.61	9.48±0.61	9.63±0.82	9.48±0.55	9.43±0.49
gram/deciliter	L	9.00±0.91	8.38±0.75	7.88±0.48	8.25±0.65	8.63±0.75
	X	11.13±0.85	10.38±0.75	9.50±0.41	9.63±0.48	10.63±0.75
	C	27.75±1.26	28.50±1.73	28.00±1.41	27.75±1.26	27.75±1.26
PCV (%)	L	26.75±0.96	24.75±1.50	23.50±1.29	24.25±0.96	25.25±0.96
	X	25.50±1.29	24.25±0.96	23.75±0.96	23.25±0.96	24.75±0.96
	C	6.16±0.36	6.16±0.36	6.18±0.34	6.15±0.33	6.16±0.36
TEC (10^6/mm^3)	L	6.06±0.21	5.80±0.29	5.56±0.22	5.40±0.22	5.83±0.21
	X	6.20±0.22	5.98±0.22	5.68±0.22	5.55±0.13	5.93±0.19

HBC = Hemoglobin concentration; gm/dl = gram/deciliter; PCV = Packed cell volume; TEC = Total erythrocyte count;

4.4. Adverse effects

In this study, male cattle calves of both groups were investigated carefully even after recovery whether some complications were present or not even some information was asked the animal owners the next day. There were no post-anesthetic complications in the feeding system, excretion, and respiration. The absence of complication does not indicate that the anesthetic drug has no problem but it indicates appropriate preparation before injection and following the correct procedure and carrying of the calves until full recovery.

CHAPTER V

5. DISCUSSION

This study analyzed the effects of epidural administration of lidocaine and xylazine on the clinico-physiological and hematological parameters of male cattle calves. Epidural anesthesia is a useful technique in ruminant animals that is widely used in conjunction with not only abdominal surgeries but also perineal surgeries and procedures (Skarda, 1996). It is a simple, inexpensive, and effective way to prevent or control pain in the anus, vulva, perineum, tail, caudal udders, scrotal region, and upper pelvic limb surgeries (Ismail 2016). When epidurally administered, lidocaine and xylazine have different mechanisms of action for analgesia. Lidocaine is a local anesthetic that acts on the cell membrane sodium channels by inhibiting propagation and conduction of nerve impulses (Aminkov and Zlateva, 2004), and xylazine is an alpha-2 adrenoceptor agonist that produces an analgesic effect due to the inhibition of the release of substance P, which is involved in pain sensation at level of substantial gelatinous of the dorsal horn of the spinal cord (Singh, Pratap, Kinjavdekar, Aithal, Singh, Pathak, 2006).

In this study, caudal epidural analgesia was satisfactorily performed at a dose of approximately 0.22mg/kg Lidocaine 2% and 0.03 mg/kg xylazine. The injection was made very comfortable in the first intercoccygeal space in a standing position. The onset of analgesia and the analgesic efficacy of lidocaine and xylazine epidurally administered to male cattle calves were evaluated.

In the current study, the onset of analgesia was produced more rapidly in Group L as compared to Group X in all-male cattle calves. Similar findings have also been reported for buffalo (Saifzadeh *et al.*, 2007) and Llamas (Molaei *et al.*, 2010) after administration of lidocaine and xylazine.

Moreover, the duration of analgesia was significantly longer in Group X as compared to Group L in all-male cattle calves. Present results are supported by other researchers who reported that the durations of epidural analgesia in camels were observed significantly longer by the administration of xylazine into the epidural space as compared to lidocaine (Molaei *et al.*, 2010).

In animals, both Group L and Group X non-significant decrease in heart rate was observed at 10 to 60 minutes after the onset of action and then increased non-significantly at 90 minutes as compared to the baseline value. Similar findings were observed by (Shendage, 2015) and (Kumar *et al.* 2020) with lidocaine under paravertebral anesthesia in bovine and following epidural administration of xylazine in horses (LeBlanc and Eberhart, 1990). In contrast to the present study (Olaifa *et al.*, 2009) observed a significant increase in heart rate after 30 minutes of administration of lidocaine in distal paravertebral anesthesia of African dwarf goats. In Group C animals, changes in heart rate were found non-significant difference and fluctuated within normal physiological limits at different time intervals.

In the animals, Group L and Group X found that respiration rate fluctuated within normal physiological limits after epidural administration in male cattle calves. In Group C, no appreciable change in the respiration rate was observed. (Shendage, 2015) in bovines using paravertebral anesthesia and (Maryam and Nasser, 2011) in sheep with thoracic-lumber anesthesia also reported that lidocaine 2% does not affect the respiration rate of animals. However, (Runa *et al.*, 2008) noted a significantly decreased respiration rate after lidocaine administration in the lumbosacral space of goats.

A significant decrease in rectal temperature was observed in animals of Groups L and Group X, from 10 to 60 minutes after injecting lidocaine and xylazine as compared to baseline. The decrease in RT was probably the result of reduced basal metabolic rate (BMR), muscle activity, and depression of the thermoregulatory center (Molaei *et al.*, 2010). Similar results of clinical parameters have been reported in camels using the same treatments (Molaei, Azari, Sakhaee, *et al*., 2010). In contrast, others (Jean *et al*., 1990; Chevalier *et al*., 2004) indicated that xylazine caused hyperthermia after epidural xylazine injection. An increase in rectal temperature has also been reported following epidural administration of xylazine in cattle (Skarda *et al*., 1990; Jean *et al.*, 1990). No significant change in rectal temperature was noticed in Group C.

In hematological parameters, there was no significant ($P > 0.05$) difference in HBC in Group L and PCV in Group X. Whereas PCV and TEC in Group L and HBC and TEC in Group X significantly ($P < 0.05$) decreased. But those values returned to near baseline levels at 120 mins in all animals. Similar findings have been reported after epidural administration of xylazine in cattle (Jean *et al*., 1990), horses (Skarda and Muir, 1994) and after epidural administration of alpha-2 adrenergic agonist in buffalo calves (Pratap *et al*., 2001). Similar observations were also recorded after the administration of lidocaine alone or in combination with xylazine for epidural analgesia in cow calves (Moulvi *et al*., 2011), and in buffalo calves (Singh *et al*., 2005). Pooling of the circulating blood cells in the spleen or other reservoirs secondary to decreased sympathetic activity could be the reason for the decrease in those parameters (Sharda *et al*., 2008). It might be also due to the shifting of fluids from the extravascular compartment to the intravascular compartment to maintain normal cardiac output during the period of anesthesia (Wagner *et al*., 1991).

The observations of various hematological parameters recorded in this study suggested that the alterations in these parameters recorded at various time intervals following epidural injection of xylazine and lidocaine were not of great magnitude. The changes were transient and more or less the same in animals of all the groups and returned to base levels within 120 min after anesthesia. Thus, xylazine and lidocaine can be safely used for epidural anesthesia in cattle.

6. CONCLUSION AND RECOMMENDATIONS

It is concluded that the caudal epidural anesthesia is safe as compared to general anesthesia in ruminants because during general anesthesia animal may take food particle, saliva or other material into the respiratory tract due to its regurgitating ability. The epidural injection of lidocaine produced early onset and shorter duration of epidural analgesia than xylazine. However, xylazine produced slow onset of analgesia but it produces longer analgesic effects as compared to lidocaine. The transient cardiopulmonary and hematological parameters recorded during observation period were well tolerated by male cattle calves. Thus, the recovery of animals in all the treatment groups was smooth, without any excitement and uncomplicated.

Therefore, the following recommendations are forwarded based on the present findings:

- Lidocaine and xylazine can be safely used for caudal epidural analgesia in male cattle calves under field conditions.
- Xylazine may be used in clinical practice for complete (longer) and safe regional analgesic effects for surgical interventions in male cattle calves.
- Further studies using latest technology are required to properly evaluate and document the anesthetic effect of lidocaine and xylazine in the clinico-physiological and hematological parameters.

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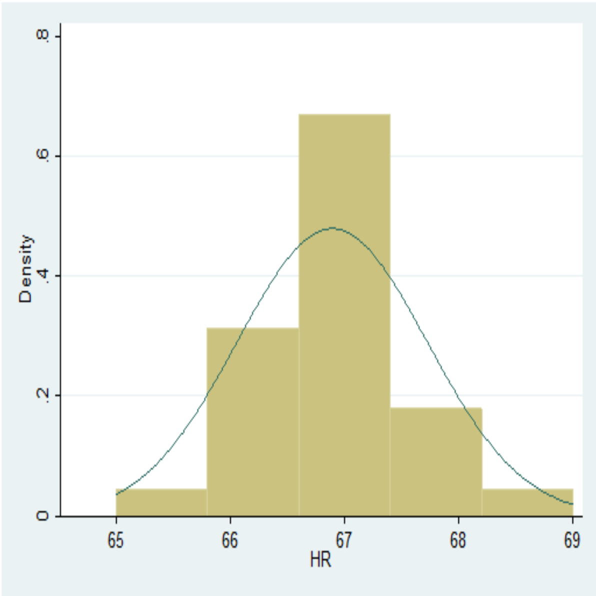
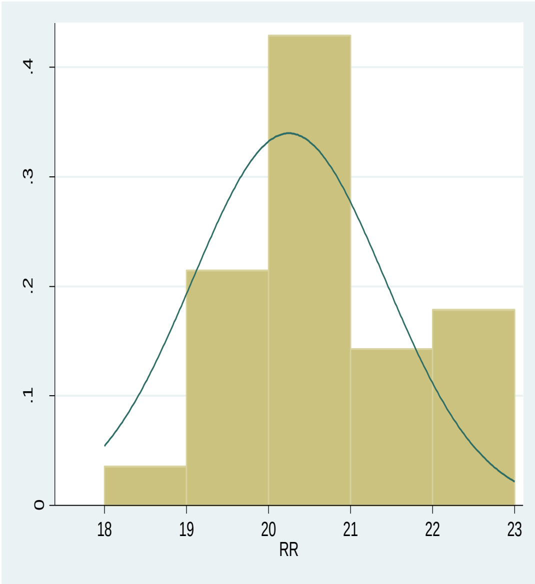
8. ANNEXES

Assumptions for the Statistical Analysis

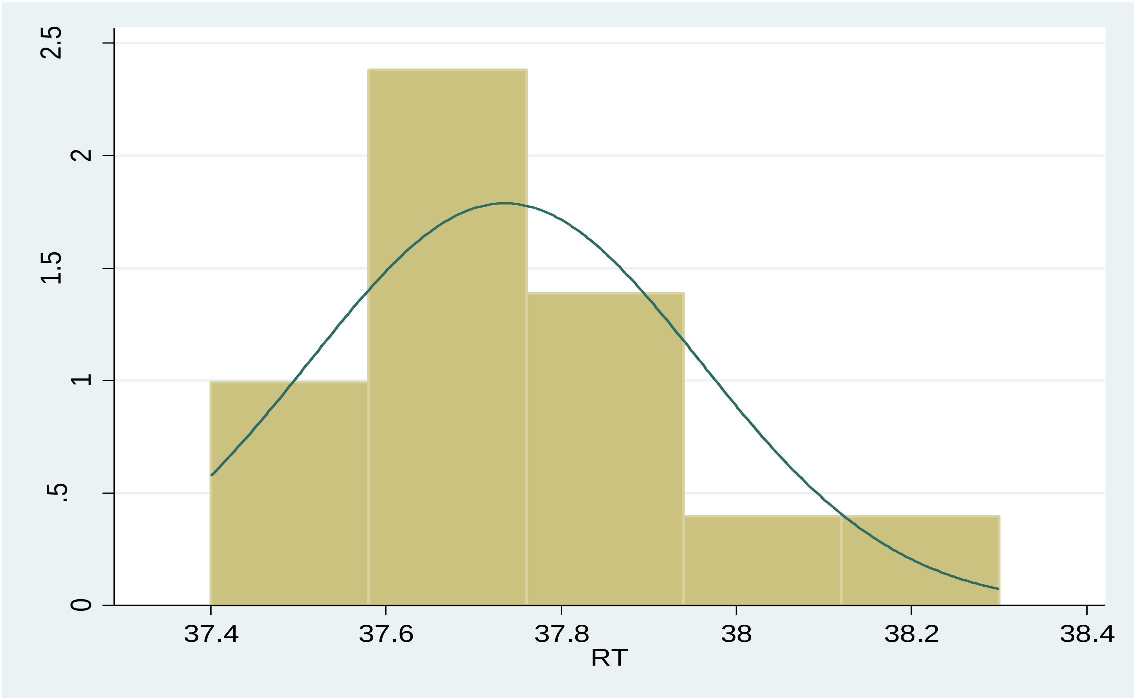
Heart rate

Respiration rate

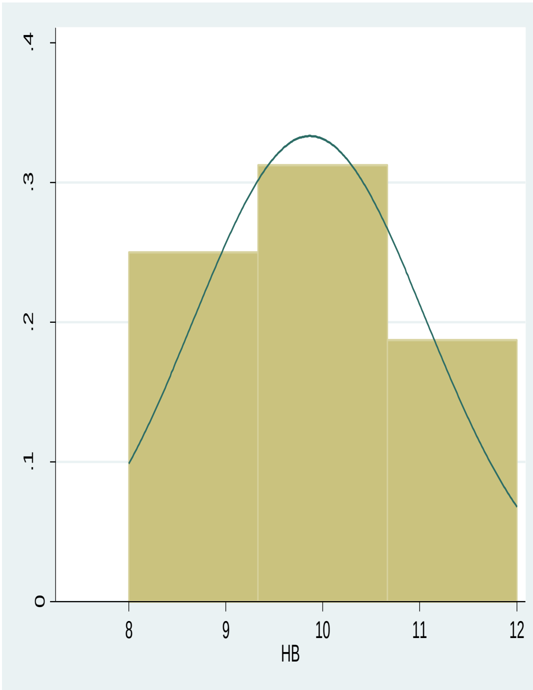




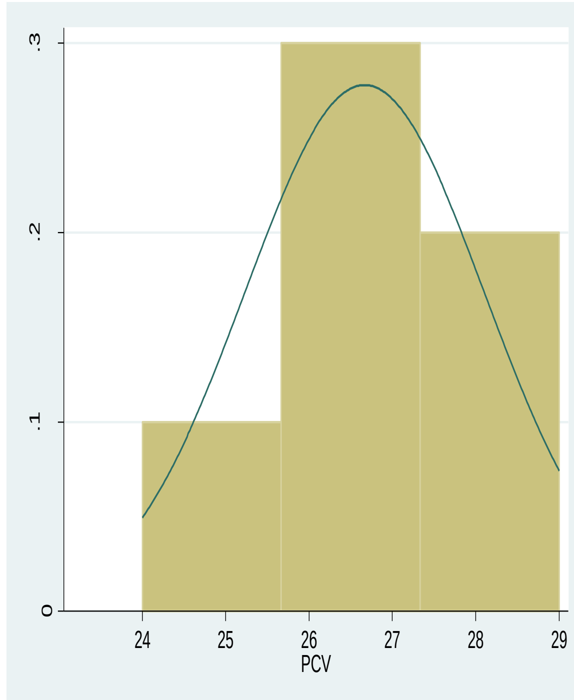
Rectal temperature



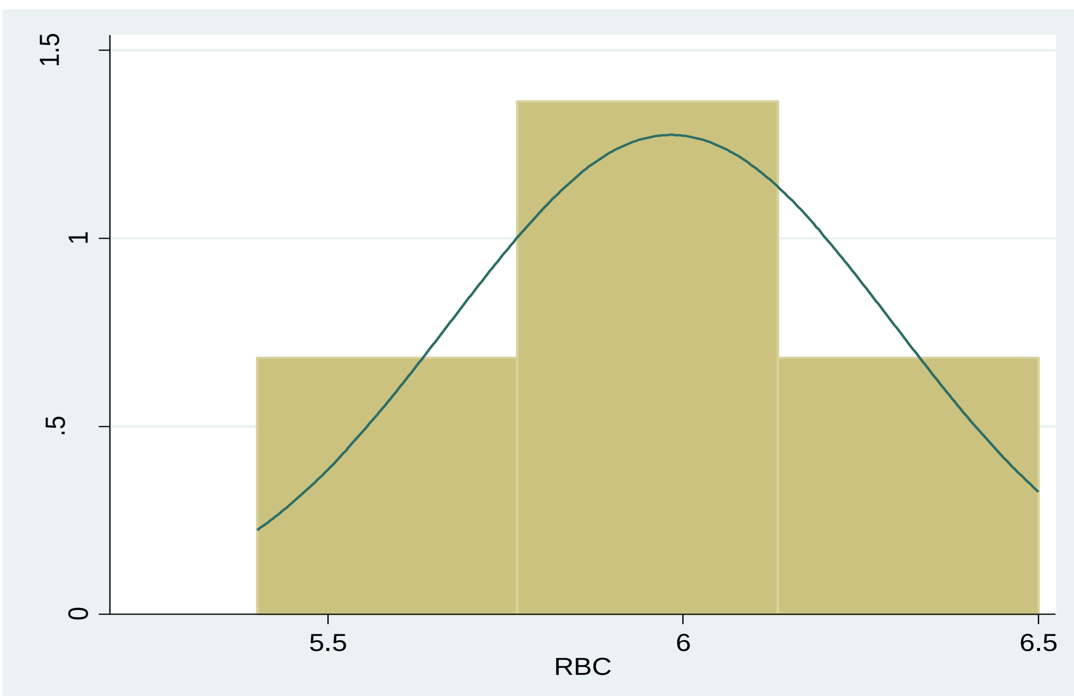
Hemoglobin concentration



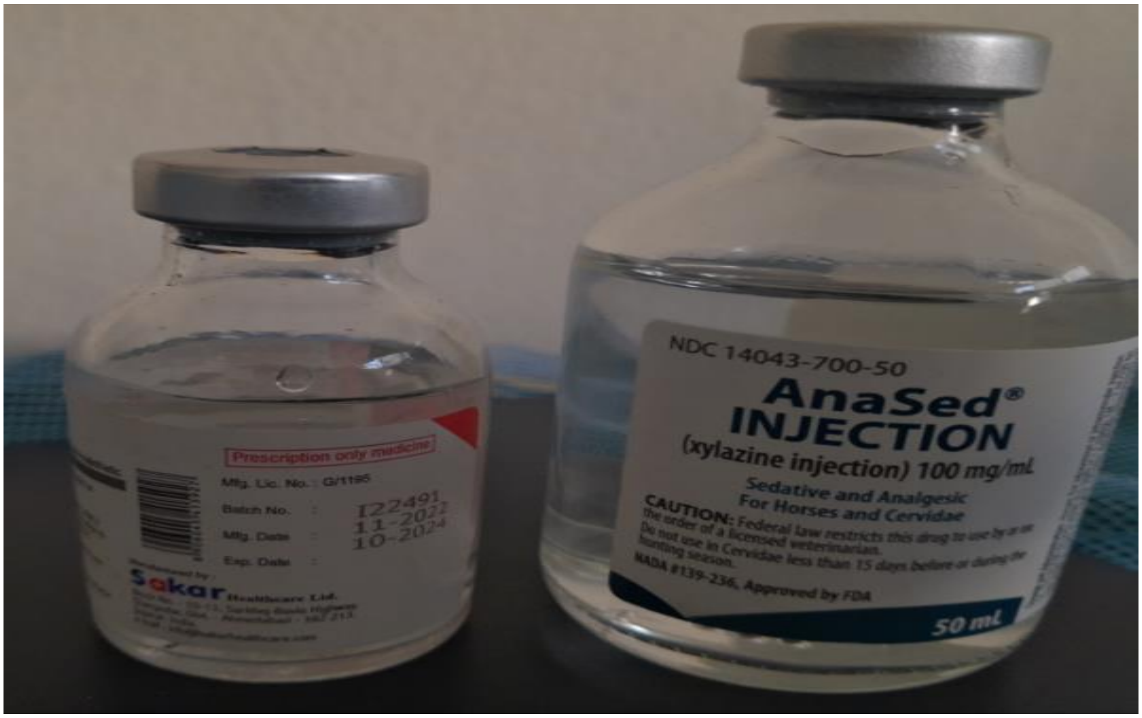
paced cell volume (PCV)

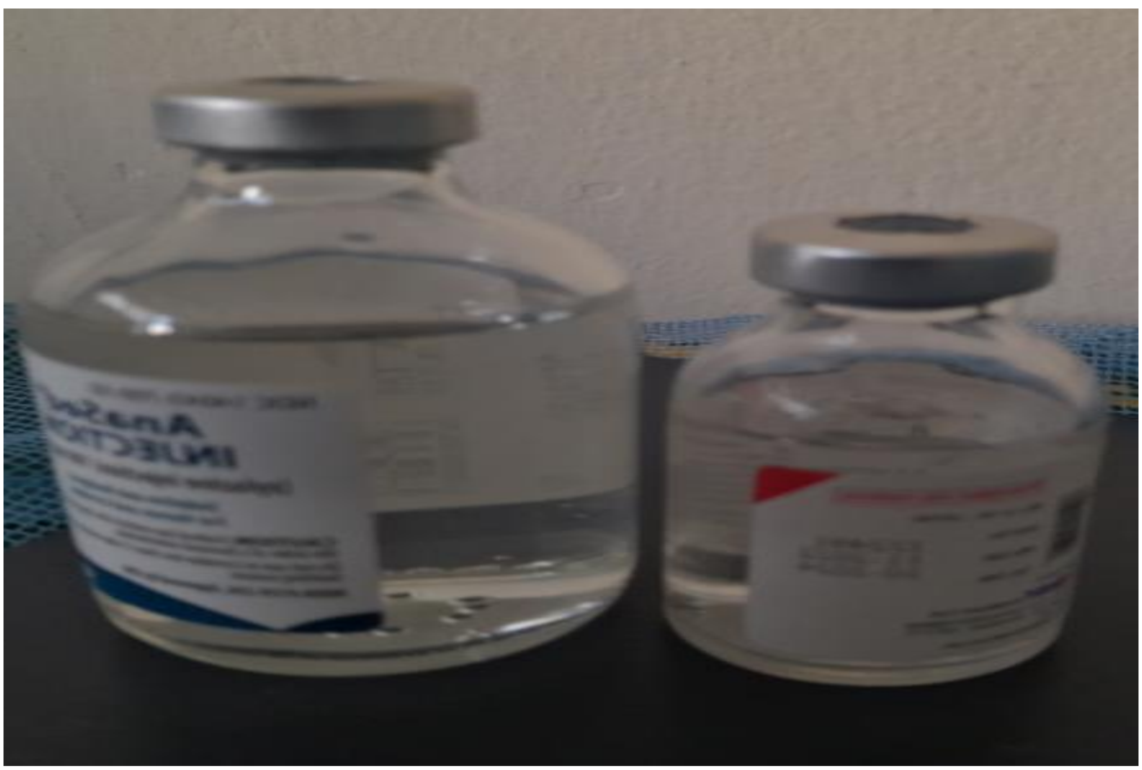


Red blood cell count



Anesthetic agents (lidocaine and xylazine) used in the experiment



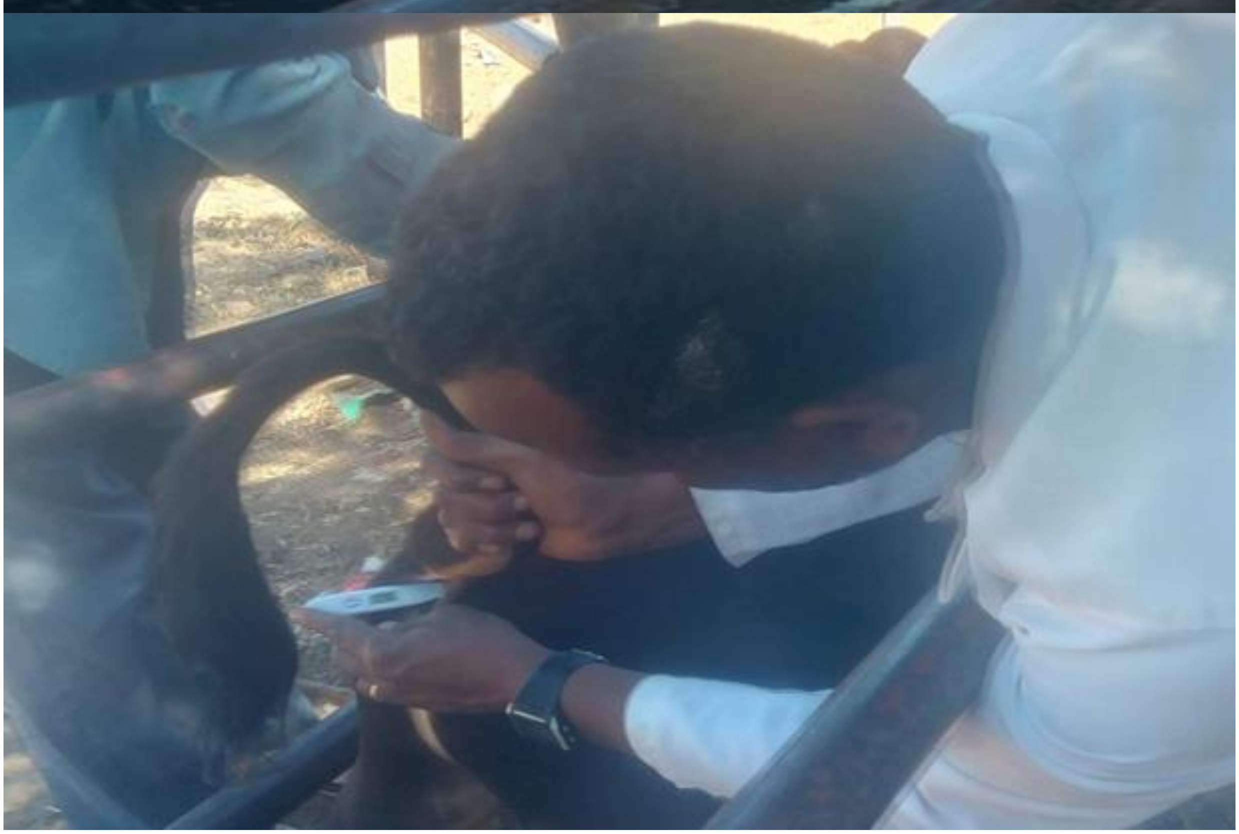


Preparation of the animals

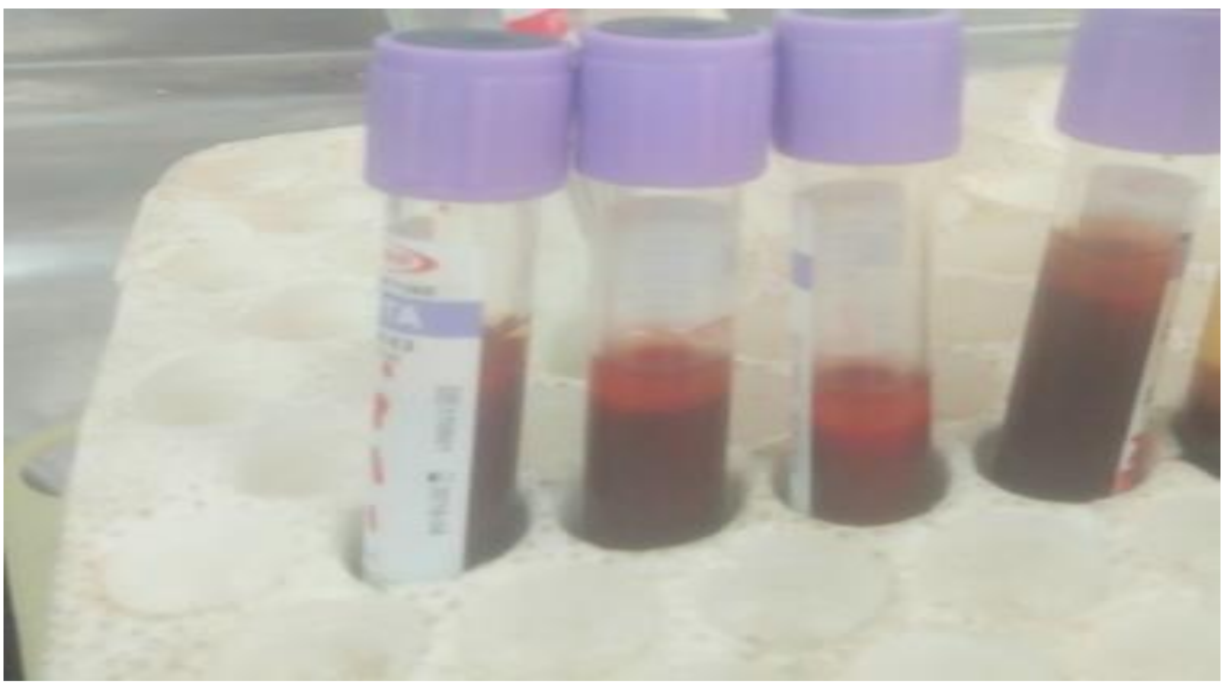



Administration of drugs (anesthesia)

Monitoring of vital signs (rectal temperature)



Blood collection



Laboratory experiment