Comparison of Anesthetic Potency and Cardiopulmonary Effects of Halothane and Isoflurane Anesthesia in Small Ruminants

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This is to certify that we have examined the above Master's thesis and have found that it is complete and satisfactory in all respects, and all revisions required by the thesis examination committee have been made

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Dedicated To Lord Krishna and My Beloved Parents

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The Author

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Table of Contents

List of Tables

List of Figures

List of abbreviations and symbols

CVASU	Chattogram Veterinary and Animal Sciences University
SAQTVH	Shahidul Alam Quadery Teaching Veterinary Hospital
MAC	Minimum Alveolar Concentration
mm	Millimetre
µg	Microgram
mg	Milligram
kg	Kilogram
BW	Body weight
L/min	Litre per minute
mL/min	Millilitre per minute
HR	Heart rate
RR	Respiratory rate
SAP	Systolic arterial pressure
MAP	Mean Arterial Pressure
DAP	Diastolic Arterial Pressure
SPO2	Oxygen saturation
@	At the rate of
%	Percentage
˚C	Degree Celsius
˚F	Degree Fahrenheit
<	Less than
>	Greater than
et al.	And his associates
et cetera	And the rest
WHO	World Health Organization
MS	Master of Science
Vs.	Versus

Abstract

This study compared the anesthetic potency and cardiopulmonary effects between halothane and isoflurane in 20 goats during routine surgery. The goats were randomly divided into two groups: HAL (n=10) and ISO (n=10), premedicated with diazepam (0.5mg/kg) intravenously, and induced by propofol (3mg/kg). Anesthesia was maintained either with halothane or isoflurane in oxygen at a total gas flow rate of 20ml/kg/min. During surgery heart rate, respiratory rate, non-invasive blood pressure, rectal temperature and oxygen hemoglobin saturation were monitored and recorded. According to the patient's response (such as blood pressure, eye position, respiratory and heart rate) to surgical stimulation, anesthetic concentration was adjusted. At the recovery stage, first head movement, sternal recumbency, ability to stand up were observed and recorded. Rapid and smooth recoveries were found in isoflurane anesthesia in comparison to halothane. Heart rate, rectal temperature, systolic arterial pressure, diastolic arterial pressure and mean arterial pressure were decreased significantly ($p < 0.05$) in HAL group. There was no significant ($p > 0.05$) differences comparing respiratory rate and oxygen saturation between the two groups. From this study, it was determined that isoflurane anesthesia in small ruminants provides a shorter and safer recovery with maximum preservation of cardiovascular and pulmonary functions. Therefore, isoflurane anesthesia can be preferred to halothane for routine anesthesia in small ruminants.

Keywords: Halothane, Isoflurane, Inhalation anesthesia, Ruminants

Chapter 1

Introduction

Halothane and isoflurane are more frequently used inhalant anesthetics in small ruminants for the maintenance of anesthesia (Mohamadnia *et al*., 2008). Halothane is a potent, nonflammable, nonirritating halogenated hydrocarbon (West *et al*., 2014). It possesses minimum alveolar concentration (MAC) 1.3 to 1.4 in small ruminants and saturated vapor pressure of 240 mm Hg at 20˚C (Hall *et al*., 2014). Halothane has been used in cattle (Rugh *et al*., 1985; Matthews *et al*., 1986; Riazuddin *et al.,* 2004; Gibson *et al*., 2009), calves (Steffey and Howland, 1979), and water buffaloes (Bose and Kohli, 1983) both as induction and maintenance agent.

Isoflurane is stable, potent halogenated ether (Tranquilli, 1986). The minimum alveolar concentration of isoflurane in small ruminants is 1.5 to 1.62 and saturated vapor pressure is 236 mm Hg at 20˚C (Hall *et al*., 2014). Isoflurane has been studied in cattle (Cantalapiedra *et al*., 2000; Riazuddin *et al*., 2004), calves (Kerr *et al*., 2007; Vesal *et al*., 2011; Offinger *et al*., 2012), water buffalo (Singh *et al*., 2013) and African buffalo (Stegmann, 2004).

Although halothane and isoflurane have analogous physicochemical properties, vapor pressure and molecular weight; induction and recovery is more swift in isoflurane than halothane due to the lower coefficient of solubility in blood (Natalini and Pires, 2000; Furtado and Andrade, 2013).

Being halogenated anesthetics, halothane and isoflurane can alter the cardiac rate and rhythm (Nakaigawa *et al.,* 1995). The cardiopulmonary effect and anesthetic potency of both halothane and isoflurane have been described in cattle (Greene *et al*., 1988), sheep (Brett *et al*., 1987; Hikasa *et al*., 2000) and goats (Antognini and Eisele, 1993; Hikasa *et*

al., 1998a). Halothane produces a potent cardiopulmonary depression (Eger *et al.*, 1970). The corresponding depletion in cardiac output, systemic arterial pressure, stroke volume and ventricular work is found with increased concentration of halothane (Steffey and Howland, 1979). In ruminants, halothane sensitizes the myocardium to cathecolamines which is reversible by alpha-blocking agents like acepromazine (Rezahani *et al*., 1977; Tranquilli *et al*., 1985). Halothane produces ventilation depression in ruminants (Tranquilli, 1986). Thirty-four percent (34%) depression in minute ventilation and 59 percent increased airway resistance by 0.75 MAC halothane was reported in lambs during spontaneous breathing (Robinson *et al*., 1985).

Isoflurane has been found to have low blood solubility, low biodegradability and produce less myocardial depressant properties than halothane (Merin *et al*., 1991; Eger, 1981 and Wade *et al*., 1981). Unlike halothane, isoflurane does not sensitize the myocardium to epinephrine and is barely arrhythmogenic (Tranquilli, 1986).

Surgical procedures in small ruminants are generally performed under physical restraining in conjunction with sedation and local or regional anesthesia. Because of the four-stomach configuration of small ruminants, they are susceptible to bloat and the regurgitation of gut contents when recumbent, with potentially fatal consequences. So, rapid recovery from anaesthesia is advantageous in small ruminants. Induction and maintenance of anesthesia can be achieved by the use of all injectable drugs or a combination of injectable premedication and inhalant maintenance. Premedications are recommended for goats to keep them calm at the time of administering induction agents (Galatos, 2011). Along with a rapid and smooth induction, propofol provides easy intubation in small ruminants (Reid *et al.,* 1993; Dzikiti *et al,*. 2009; Dzikiti *et al,*. 2010; Larenza *et al.*, 2005; Prassinos *et al*., 2005). After induction, a cuffed endotracheal tube is intubated to prevent aspiration of ruminal contents (Taylor, 1991; Reid *et al.,* 1993; Dzikiti, 2010; Galatos, 2011). Because of the long, narrow oral cavity and distant laryngeal opening, endotracheal intubation in small ruminants is difficult (Dzikiti, 2013). Visualization is facilitated by using a long-bladed laryngoscope along with a non-flexible stylet for easier tube placement into trachea (Taylor, 1991; Taylor, 1991; Caulkett, 2003).

Though short and non-painful surgical procedures can be executed with injectable drugs for both induction and maintenance, prolonged and painful procedures should be accomplished with injectable induction and inhalant maintenance (Kaiser, 2007). For complex, and longer procedures, such as orthopedic surgery, prepubic tendon rupture, diaphragmatic hernia or ventral hernia, anesthesia must be maintained with inhalant anesthetics (Riazuddin *et al*., 2004). In comparison to injectable anesthesia, inhalant anesthesia causes faster changes in depth of anesthesia, earlier shift of central nervous system (CNS) depression, quick elimination through the lungs, faster recovery from anesthesia and minor risk of overdosing (Bodh *et al*., 2014).

Therefore, the present study was conducted with the aim to evaluate and compare the effects of halothane and isoflurane anesthesia on certain cardiopulmonary and hemodynamic parameters along with recovery characteristics in small ruminants under a variety of surgical procedures in clinical settings.

Chapter 2

Review of literature

General anesthesia in small ruminants (sheep and goats) requires special attention due to anatomic and physiologic differences from dogs, cats, and horses. Although the purposes of raising ruminants are meat, milk, skin, fibre, teaching and research, small ruminants are specially reared as companion animals (Carroll and Hartsfield, 1996). Sheep and goats have become popular house pets in the last few years. Although the commercial value of these goats may not be extraordinary, their owners are usually willing to spend more for veterinary care. Small ruminants are also preferred in various experimental studies like orthopedic, cardiovascular, cerebrovascular, and respiratory studies (Carroll *et al*., 1998; Kastner *et al*., 2001; Kutter *et al*., 2006). Some ruminants are undergoing medical and surgical correction beyond their economic value as food animals. So many drugs that were restricted only to companion animals or horses are now being used to ruminants (Carroll and Hartsfield, 1996).

2.1 General anesthesia

Anesthesia is the term derived from the Greek term ‘anaisthaesia’ which means ‘insensibility’. Anesthesia can be defined as the loss of sensation in a body part or in the whole body by inducing drugs that depress the activity of nervous tissue either locally, regionally, or generally (Muir *et al*., 2013).

General anesthesia is drug-induced unconsciousness or loss of sensation which is characterized by controlled but reversible depression of the CNS, muscle relaxation, analgesia and suppression of stress (Muir *et al*., 2013). General anesthesia can be produced with a single drug or a combination of drugs. Also, it can be induced and maintained with either injectable or inhalation anesthetics or both.

General anesthesia in farm animal species with injectable or inhalant anesthetics depends on some factors such as the surgical procedure, duration of the procedure, availability of inhalation anesthetic equipment, knowledge of veterinarians with the anesthetic techniques and the costs of anesthetics (Lin and Walz, 2014).

2.2 Basic requirements for anaesthesia in small ruminants

Anesthetic management in small ruminants is usually not complicated, except for primary notable risk of regurgitation with potentially fatal pulmonary aspiration (Hall *et al*., 2001). Mature ruminants have the four-compartmental stomach with large rumen which does not easily emptied (Riebold, 2007). Rumen fermentation and risk of regurgitation are decreased if food is withheld for 12-18 h but it rarely reduces the volume of ruminal contents (Abrahamsen, 2008; Taylor, 1991; Valverde and Doherty, 2008). For small ruminants, water is withheld for 6-12h (Fulton *et al*., 1994).

After induction of general anesthesia in mature small ruminants, an endotracheal tube must be placed with the cuff inflation even after taking precautions suggested above to prevent aspiration of rumen contents (Abrahamsen, 2008; Galatos, 2011; Riebold, 2007). Because of the long, narrow oral cavity and distant laryngeal opening endotracheal intubation in goats and sheep is difficult. But after facilitating visualization by using a long-bladed laryngoscope, placement of the tube into the trachea becomes much easier (Caulkett, 2003; Taylor, 1991).

As hypoxaemia develops commonly on goats with general anesthesia, a physical examination should be performed prior to the anesthetic procedure (Hall *et al*., 2001). When anesthetized in dorsal or lateral recumbent position, gas accumulates in rumen as the normal eructation is hampered. As a result, ruminal tympany or bloat occurs and the distended rumen causes the lung capacity decease by exerting pressure on the diaphragm (Fulton *et al*., 1994; Galatos, 2011). To reduce the risk of hypoxemia and hypercarbia and to resolve gaseous distension, a stomach tube can be passed after intubation (Riebold, 2007).

Oxygen supplementation, intravenous fluid for maintenance and replacement needs, heat conservation and supplementation should be included as a supportive therapy during anesthesia (Abrahamsen, 2008). For maintenance of fluid a balanced electrolyte solution can be given through intravenous catheter (Fulton *et al.,* 1994).

Premedication is recommended in small ruminants before administering induction agents for making them calm (Galatos, 2011).

2.3 Preoperative preparation

For general anesthesia in ruminants, preoperative preparation is condemnatory. Before anesthesia, withholding of food and water, detailed physical examination, blood test, serum biochemistry profile, precise bodyweight should be taken. For rapid and safe administration of anesthetics and fluids, venous catheterization can be performed. Fasting should be strictly maintained in patients undergoing elective surgery. Aspiration of rumen content and regurgitation can become fatal and to reduce the fermentation in the rumen and to reduce tympany, fasting is most important (Thurmon and Benson, 1986). Besides regurgitation hypoventilation and hypoxemia are great prospect in food animals (Blaze *et al*., 1988).

In sheep and goats, a usual recommendation for preoperative fasting is 24-hour without water restriction (Ewing, 1990; Gray, McDonell, 1986; Smith and Sherman, 1994). Due to the development of metabolic acidosis with longer fasting, long time fasting is not recommended in pregnant sheep and goats (Ewing, 1990; Gray, McDonell, 1986; Smith and Sherman, 1994).

For longer fasting, more liquid ingesta is elevated that may raise the risk of regurgitation (McDonell, 1986).

Without supplementation of oxygen hypoventilation and hypoxemia is common when the animals are positioned head down in cradles. During general anesthesia all ruminants must be orotracheally intubated to protect their airway by inflation of the endotracheal tube's cuff and for draining of saliva and regurgitated material head should be positioned.

Pre-anesthetics can be classified as anticholinergics, tranquilizers, sedatives, and analgesics. In ruminants, anticholinergics are not generally recommended for ruminants (Alibhai *et al*., 1994; Short, 1986 and Trim, 1987). High and repeated dose of atropine is needed in small ruminants to decrease salivation (Gray and McDonell, 1986; Thurmon and Benson, 1986). Anticholinergic causes the saliva and respiratory secretion more viscous that encourages airway obstruction (Short, 1986; Trim, 1987). Sedatives and tranquilizers help in restraining and handling of grumpy animals. Most pre-anesthetics such as sedatives, tranquilizers and analgesics not only reduce the successive anesthetic drugs but also improve the stress response to anesthesia (Carroll and Hartsfield, 1996). It

also makes the safer induction of anesthesia, lower incidence and intensity of adverse effects, anticipates preemptive analgesia and makes the recovery smooth (Valverde and Doherty, 2008; Riebold, 2007).

2.3.1 Diazepam

Benzodiazepines can act as anxiolytic, mild sedatives, muscle relaxant and anticonvulsant except for analgesic property (Valverde and Doherty, 2008; Riebold, 2007; Hall *et al*., 2001). As the cardiovascular and respiratory effects of this groups are minimal and transient (Valverde and Doherty, 2008), they can be safely used in animals with cardiopulmonary diseases. Drugs of this group may produce minute ventilation and transient hypoxemia (Valverde and Doherty, 2008). Diazepam is one of the most commonly used drugs in benzodiazepines group (Galatos, 2011; Posner, 2007). It is fast-acting and short elimination half-life (Lemke, 2007; Posner, 2007). As diazepam is water insoluble, it is delivered with an organic solvent propylene glycol that causes pain and unpredictable absorption when administered subcutaneously or intramuscularly (Posner, 2007). Due to irritant property and unpredictable absorption and degree of sedation after intramuscular administration (Valverde and Doherty, 2008; Hall *et al*., 2001), a slow intravenous route is preferable to avoid momentary excitement (Gray and McDonell, 1986). In small ruminants, diazepam is usually administered at doses of 0.1 mg/kg – 0.5 mg/kg, intravenously for premedication (Dzikiti *et al.*, 2009; Ghurashi *et al.*, 2009; Lemke, 2007). Diazepam is commonly used as mild tranquilizers, anticonvulsants, potent muscle relaxants and also produces mild, transient cardiovascular and respiratory effects (Galatos, 2011; Lemke, 2007).

2.4 Induction

General anesthesia in ruminants can be induced by musk induction or by injectable anesthetics and the maintenance of general anesthesia can be done with either barbiturate, non-barbiturates, dissociative anesthetics or inhalant anesthetic agents (Trim, 1981). Facemask induction is preferable for the small ruminants weighing less than 50 to 100 kg (Riebold, 2007) and especially for very young and debilitated animals (Gray and McDonell, 1986; Lin and Pugh, 2002). But this technique is not recommended generally for large, healthy and adult animals (Lin and Pugh, 2002) as the induction is delayed, risk

of regurgitation and aspiration is high, intubation of the endotracheal tube is not feasible and consumption of anesthetics and environmental pollution are extravagant (Valverde and Doherty, 2008). Anesthesia induced with injectable anesthetics and maintained with inhalation anesthetics is preferable (Galatos, 2011).

2.4.1 Propofol

Propofol is a non-barbiturate, non-steroidal sedative and hypnotic agent that can be used in small ruminants providing short periods of anesthesia (5–10 min). It can be safely used in small ruminants due to its short half–life, rapid metabolism and absence of accumulation in the body (Reid *et al*., 1993; Glowaski and Wetmore, 1999; Muir, 2007; White, 2008). In unsedated ruminants dose is 4-6 mg/kg intravenously (Taylor, 1991; waterman, 1988; Nolan *et al*., 1991; Handel *et al*., 1991). Propofol facilitates easy intubation in small ruminants by providing rapid and smooth induction (Dzikiti *et al.*, 2010; Dzikiti *et al.,* 2009; Larenza *et al.*, 2005; Prassinos *et al*., 2005; Reid *et al.*, 1993).

In propofol (4mg/kg) induced and halothane maintained anesthesia in goats for 15 to 45 minutes were shown to take about 5, 9 and 14 minutes from the end of halothane to extubation, to sternal recumbency and standing respectively (Rield *et al*., 1993). Apnea (Pablo *et al*., 1995; Rields *et al*., 1993), hypoventilation (Carroll *et al*., 1995), regurgitation (Riel*det al*., 1993), the myoclonic activity of the face and limbs (Pablo *et al*., 1995) may be found with propofol anesthesia.

Rapid injection of propofol may cause induction apnea more than other general anesthetics (Bettschart- Wolfensberger *et al*., 2000; Carroll *et al*., 1998; Langley and Heel, 1988; Pablo *et al*., 1997; Galatos, 2011). But this complication can be reduced by slow administration (Riebold, 2015). Recovery usually occurs within 15 minutes (Correia *et al*., 1996). Dose-dependent cardiovascular and respiratory depression may be found for propofol and monitoring with necessary corrective measures such as intravenous fluid, ventilation support should be provided (Hodgkinson and Dawson, 2007).

2.5 Endotracheal intubation

Endotracheal intubation is indispensable not only during inhalation anesthesia but also during injectable anesthesia, which is maintained for more than 10 minutes (Galatos,

2011). It is mandatory to prevent the ruminal contents or saliva aspiration and to allow unrestricted oxygen administration and assisted or controlled ventilation when apnea is found (Thurmon and Benson, 1993; Valverde and Doherty, 2008). In sufficiently anesthetized animals, intubation should be done quickly holding the animal in sternal recumbency with a fully extended head and neck to lessen the risk of aspiration. During intubation, if regurgitation takes place the animal should be immediately kept in lateral recumbency with the head lowered for draining the fluids and to excavate material out of the mouth (Galatos, 2011).

Before intubation, a suitable endotracheal tube should be selected and a somewhat smaller and larger tube should be at hand. Tracheal diameter can be set on by palpating the trachea (Tranquilli, 1986). The internal diameter of the endotracheal tube is the major factor of breathing resistant. Though thin-walled tubes are preferable, the cuff should not be overinflated crumpling the tube. In small ruminants, 5 to 14 mm internal diameter tubes are used where the sheep require tubes 1 to 2 sizes larger than the goats of same bodyweight require (Thurmon and Benson, 1993; Valverde and Doherty, 2008; Gray and McDonell, 1986).

For endotracheal intubation numerous techniques have been expressed (Thurmon and Benson, 1993, Hall *et al*., 2001, Gray and McDonell, 1986). Orotracheal intubation is more preferred than nasotracheal intubation (Valverde and Doherty, 2008). Endotracheal intubation is easier with the help of a long-bladed (25 to 35cm) laryngoscope as it aid in direct vision. To facilitate intubation, a guide tube or placement of animals into dorsal recumbency makes it easier (Hall *et al*., 2001; Gray and McDonell, 1986). Blind intubation can be executed in absence of laryngoscope keeping the animal in sternal or lateral recumbency grasping the larynx externally with one hand and the endotracheal tube is inserted into by the other hand (Gray and McDonell, 1986). The cuff is inflated and the tube is left in place after introducing the endotracheal tube until the swallowing reflex is retrieved during recovery.

2.6 Inhalant anesthetics

Ether, halothane and members of the ‘flurane’ family (methoxiflurane, isoflurane, sevoflurane, desflurane and enflurane) are the most commonly used inhalant anesthetics

in animals (Furtado and Andrade, 2013). In small ruminants most commonly used inhalant anesthetic both for induction and maintenance is halothane and isoflurane (Taylor, 1991; Mohamadina *et al*., 2008). Less commonly used in ruminants are enflurane and methoxyflurane (Carroll and Hartsfield, 1996). In ruminants, nitrous oxide is not recommended as it increases the risk of ruminaltympany (Ivany and Muir, 2004). Isoflurane is comparatively more chosen than halothane, especially in compromised patients as it does not sensitize the myocardium to catecholamine-induced arrhythmias, less dependent on metabolism for elimination (Valverde and Doherty, 2008; Carroll and Hartsfield, 1996) and also provides faster induction (Valverde and Doherty, 2008) and recovery (Hisaka *et al*., 2002).

Inhalant anesthetics are preferable to injectable agents for many advantages such as rapid recovery, return from anesthetic hypothermia, lower incidence of death, undergo little metabolism, expelled from the body during respiration and also the manipulation and control ofthe concentration of inhalant agents is easier (Murrell *et al*., 2008; Furtado and Andrade, 2013).

Inhalation anesthesia is the safest and satisfactory for very young or aged animals, pregnant debilitated patients or for the prolonged (>1hour) and complicated surgery (Gray and McDonell, 1986; Thurmon and Benson, 1993; Carroll and Hartsfield, 1996; Lin and Pugh, 2002; Ivany and Muir, 2004).

For small ruminants up to 140 kg (300 lb) bodyweight, the small animal anesthetic machine can be used to orchestrate the anesthetics using same vaporizer settings for maintenance that would be used for a large canine patient (Trim, 1981). For induction with halothane, isoflurane and sevoflurane, the vaporizer should be set at 3% to 5%, 2% to 5% and 4% to 6% respectively and during maintenance, the vaporizer setting should be adjusted to 1% to 2%, 1.5% to 3%, or 2.5% to 4% for halothane, isoflurane, or sevoflurane, respectively (Rebold, 2007; Hall *et al*., 2001).

5 to 8 L/min flow rate of oxygen in adult cattle and 2 to 4 L/min in small ruminants should be provided after induction and 3-5 L/min for adult cattle and 1-2L/min for small ruminants are provided for maintenance (Carroll and Hartsfield, 1996).

2.7 Mechanism of action of Inhalation anesthetics

Inhalant anesthetics produce sedation through the depression of spinal cord function. They increase the activity of inhibitory neuronal pathways that are dependent on the γ-aminobutyric acid type A (GABA-A) receptor and glycine. As a result, the excitatory pathways which are dependent on the activation of neuronal nicotinic receptors for acetylcholine, serotonin and glutamate are inhibited. And thus amnesia is produced by the inhalant anesthetics (Campagna *et al*., 2003).

2.8 Pharmacokinetics of inhalant anesthetics

2.8.1 Anesthetic Uptake and Distribution

The movement of anesthetic gas is driven by a series of partial pressure gradients from the starting at vaporizer and it continues in the breathing circuit, the airways, alveoli, blood and ends in the tissues.

The anesthetic gas movement continues until the partial pressure is equal throughout the system. The alveolar partial pressure controls the partial pressure of the anesthetic gas in all body tissue as the lung is both entry and exit to the body. Delivery of anesthetics is sped up when the flow rates at the level of the vaporizer, and inspired anesthetic concentration and alveolar minute ventilation is increased. The uptake of the anesthetic from the alveoli into the blood depends on the Solubility, cardiac output, and the alveolar-to-venous anesthetic gradient. Solubility or partition coefficient is the affinity of the gas for a medium such as blood or adipose tissue (West *et al*., 2014). Once the equilibrium has been reached between the two phases of blood and alveolar gas, the gas partitions itself is known as blood/gas partition coefficient. The blood/gas partition coefficient of Isoflurane is approximately 1.4 (Steffey and Mama, 2007) which means when the gas partial pressures are in equilibrium, the concentration in blood will be 1.4 times greater than the concentration in the alveoli. The higher the blood/gas partition coefficient, the greater the uptake of the gas into the blood and the slower rate of rising of alveolar and blood partial pressure. It takes longer for the brain partial pressure of the gas to increase as the blood partial pressure rise is slower and results in a longer induction time.

The alveoli are more exposed to blood per unit time when the cardiac output increases. The more blood volume causes removal of more inhalant anesthetic from the alveolus which ultimately lowers the alveolar partial pressure. The gas takes longer time to reach equilibrium in between the alveoli and the brain when the partial pressure in the arterial blood is lower although the agent might be distributed faster within the body. Thus induction time is usually prolonged with high cardiac output. The differences of alveolar to venous partial pressure reflect the tissue uptake of the inhalant anesthetic. Increased uptake of the gas by the tissues causes a large difference during the induction phase.

The brain/blood coefficient denotes the partition of gas between the two phases when the equilibrium has been reached. For example, a brain/blood coefficient of 2.7 in isoflurane indicates 2.7 times greater concentration in the brain than in the blood concentration at equilibrium (Steffey and Mama, 2007).

Modern inhalant anesthetics have higher adipose/blood partition which signifies that most of the gas assembles in adipose tissue as time goes by.

As the adipose tissues have high adipose/blood partition coefficient, the partial pressure of the gas rises very slowly. This storage of inhalant anesthetics may cause delay awakening at the end of long periods of anesthesia in obese patients. Due to low blood flow in adipose tissue, anesthetics during short-duration anesthesia do not accumulate significantly in commonly experienced veterinary medicine (West *et al*., 2014).

2.8.2 Elimination of Inhaled Anesthetics

To excrete the volatile anesthetics and their metabolites lungs and kidneys are major excretory pathways (Trim, 1981). Deepening on tissue solubility the rate of induction and recovery in inhalation anesthesia varies. Though all tissue partial pressures are zero during induction, different partial pressures of anesthetics in different tissues of the body due to tissue anesthetic content. Anesthetic induction is more controllable than recovery. Elimination during anesthetic recovery occurs by exhalation or by biotransformation. Anesthetics are mainly metabolized by the enzymes in liver and kidneys. The rate of elimination via metabolism is nearly zero for nitrous oxide, 0.001% for desflurane, about 0.2% for isoflurane, 2.5% for enflurane, 5–8% for sevoflurane, 10–20% for halothane and 50% for methoxyflurane (Steffey and Mama, 2007). Inhalant anesthetics are more eliminated from the body by exhalation than by metabolism.

An increase in minute ventilation during recovery causes decrease in alveolar partial pressure of anesthetics and rising of diffusion of gradient from blood to the alveoli. As a result anesthetic with high blood/gas partition coefficients are eliminated more through lungs.

Cardiac output has effects on the elimination of anesthetics via the lungs. Increased cardiac output during induction causes an increased rate of removal of anesthetics as it slows the increasing rate of anesthetic partial pressure and thus slows induction. In case of decreased cardiac output rate of removal of anesthetics is slower, rate of rising of alveolar partial pressure and induction is faster.

Increased cardiac output during the recovery causes a rising of anesthetic returns rate to the lungs for excretion. The more the blood flow the shorter the recovery. When the cardiac output decreases, recovery will be slower as the rate of decreasing anesthetic partial pressure is reduced.

The solubility of the anesthetic agent influences the induction and recovery. High blood/gas solubility causes more partition of the anesthetics into blood than low blood/gas solubility. It is because of blood stores anesthetic agents for maintaining the partial pressure. The low blood/gas soluble anesthetic causes a faster reduction of partial pressure and reduction in recovery time as they do not partition into blood much. The anesthetics having high solubility cause high blood concentrations that takes longer to reducing partial pressure when all other factors are same.

To sum up, ventilation, cardiac output and solubility of anesthetic agents contributes to the elimination of anesthetic agents (West *et al.*, 2014).

2.9 General Pharmacological Actions of Inhalant Anesthetics

There are more similarities among the inhalant anesthetics than differences in case of their effects on vital organ systems. The paradigmatic differences are mentioned in the following.

2.9.1 Central Nervous System

Inhalant anesthetics act on the central nervous system and alter consciousness, memory and pain perception. At low MAC, inhalant anesthetics have minimal effects on cerebral blood flow and a mild to moderate decrease in cerebral metabolic requirement

for oxygen (Mielck *et al*., 1998, 1999). Nitrous oxide should not be used to anesthetize the patients with intracranial hypertension as it causes an increase in cerebral metabolic requirement for oxygen CMRO2 (Algotsson *et al*., 1992; Hoffman *et al*., 1995; Roald *et al*., 1991). In these patients, halothane is also a poor choice as it has significant effects on cerebral blood flow auto regulation (Steffey and Mama, 2007) whereas Isoflurane, sevoflurane, and desflurane have no such effects and can be chosen in these patients.

2.9.2 Cardiovascular System

Myocardial depression is caused by most inhalant anesthetics. Although halothane mostly depresses contractility, it generally affects the fewest on vascular resistance (Steffey and Mama, 2007). Other inhalant anesthetics such as isoflurane, sevoflurane, desflurane and enflurane cause vasodilatation that improves forward blood flow and maintains tissue perfusion. A sympathetic response and temporarily increase cardiac function has resulted from the rapid changes in anesthetic concentration (West *et al*., 2014).

2.9.3 Respiratory System

Respiratory acidosis is a common complication in inhalation anesthesia if assisted or controlled ventilation is not provided. It is caused by the depression of chemoreceptor response to carbon dioxide leading to an accumulation of carbon dioxide. All inhalant anesthetics may produce significant depression but the ether derivates are most depressant. In large animals significant pulmonary shunt is common. It is caused by the interference with ventilation and due to pulmonary vasoconstriction by most inhalant anesthetics (West *et al*., 2014).

2.9.4 Genitourinary system

Almost all anesthetics cause a reduction of renal perfusion and rise of antidiuretic hormone secretion. Since inhalant anesthetics are excreted by lungs and not depend on renal function, it is the safest technique in case of a patient with anuric renal failure (West *et al*., 2014).

Elevation of postpartum uterine bleeding may be caused by inhalant anesthetics and in primate it should be contemplated for their placenta feature. Inhalant anesthetics with

rapid onset and termination such as isoflurane, desflurane and nitrous oxide have been recommended during caesarian section (West *et al*., 2014).

2.10 Halothane

Halothane is a structure of 2-bromo-2-chloro-1, 1, 1-trifluoroethane and was first introduced as an anesthetic into veterinary in 1956 (Hall, 1957). It is the first inhalation anesthetics to use effectively in large animals (Hall, 2014). Halothane is used for medical and veterinary use in many areas of the world except North America and Europe and is listed as core medicine in World Health Organization's list (WHO, 2010). Halothane can be broken down by ultraviolet light and for this reason it is stored in dark bottles with a preservative named thymol.

Halothane can be used to induce anesthesia as it does not irritate the respiratory mucosa and does not cause breath holding as isoflurane (Hall, 2014).

Though halothane causes dose-dependent respiratory depression, spontaneous breathing occurs in animals in case of halothane anesthesia (Steffey, 2002). Halothane causes a dose-dependent cardiac output and arterial blood pressure depression in all mammalian species. Due to vagal activity bradycardia is common with halothane anesthesia. Also due to CO_2 accumulation from hypoxia, respiratory depression and catecholamine release halothane may induce arrhythmia. Epinephrine-induced tachyarrhythmia is produced during halothane anesthesia because of sensitization of heart (Hall, 2014). However, with time some adaptation of both respiratory and cardiovascular functions occurs (Dunlop *et al*., 1987; Steffey *et al*., 1987).

At the start of surgery blood pressure increases because of increased systemic vascular resistance (Wagner *et al.*, 1995). Supplementation with analgesics is often effective in halothane maintenance anesthesia as it is a poor analgesic, has minimal muscle relaxant effects and does not help in postoperative analgesia (Hall, 2014). During recovery in all domestic species, shivering is very common although the cause is not completely known. Like all other halogenated anesthetic agents, halothane can trigger malignant hyperthermia (Hall, 2014). More than 25% metabolism of halothane occurs in the liver. Though the increase of hepatic enzyme is not clinically important in most domestic animals, guinea pigs are reported to be particularly susceptible (Lunam *et al*., 1985) and

goats are reported to have post anesthetic fatalities along with acute liver damage (Antognini and Eisele, 1993).

Halothane is withdrawn from human anesthesia in North America and Europe due to its immune-mediated fatal fulminant hepatic failure (less than 1: 35 000 – as reported in the National Halothane Study, Bunker, 1968; Bunker *et al.*, 1969) which occurs for repeated exposure to the drug at short intervals (Elliott and Strunin, 1993). However, there is no proof of this type of hepatitis that results from halothane anesthesia in animals.

2.11 Isoflurane

Isoflurane has been used for more than 40 years in both humans and animals and due to its 'minimal residual limit' it is used in food animals in Europe. Isoflurane is 1-chloro-2-trifluoroethyl-difluoromethyl ether compound which is a structural isomer of enflurane and racemic mixture of two optical isomers (Hellebrekers, 1986; Stevens, 1972). It is a clear liquid with high volatility and does not require any preservatives. Isoflurane causes rapid induction and recovery due to its low blood solubility and low biodegradability (Eger, 1981; Wade and Steven, 1981, Hall 2014). Although Isoflurane is not suitable for mask induction as it has a pungent smell and causes coughing, airway irritation, breath-holding, maintaining stability and changing the depth of anesthesia is easy with isoflurane (Hall, 2014).

Isoflurane causes greater respiratory depression than halothane, although surgical stimulation counteracts it. A noticeable dose-dependent fall in arterial blood pressure and systemic vascular resistance is seen in isoflurane anesthesia while little myocardial depression, normal or increased heart rate is noticed (Hall *et al*., 2014). In comparison to halothane, isoflurane in oxygen anesthesia shows pink membranes which denote good peripheral blood flow. Epinephrine-induced arrhythmias are absent in isoflurane anesthesia as it does not sensitize the myocardium (Hall *et al*., 2014).

Blood flow to vital organs during isoflurane anesthesia is well maintained due to the maintenance of cardiac output along with vasodilation while at 1 MAC or less it decreases cerebral vascular resistance and cerebral metabolic rate (Young, 1992).

Very little biotransformation (approximately 0.2%) occurs in isoflurane and the main metabolites are trifluroacetic acid and inorganic fluoride. However, the risk of immune-mediated hepatitis is lower in susceptible patients than halothane. Isoflurane can induce malignant hyperthermia. Carbon monoxide is formed due to the interaction of isoflurane with dry soda lime (Kharasch, 2008).

2.12 Monitoring the anaesthetized small ruminants

To ensure an appropriate anesthetic depth and to assess peri-anesthetic complications of the digestive system (tympany, regurgitation, excessive salivation) and cardiopulmonary system (hypercarbia, hypotension, hypoxaemia), small ruminants should be monitored carefully during anesthesia (Galatos, 2011; Taylor, 1991). Small ruminants show sluggish palpebral, pedal reflexes and stable autonomic responses when they are properly anesthetized (Galatos, 2011). When deeply anesthetized, absence of palpebral and corneal reflex, dry cornea, severe bradypnoea and apnoea is observed in small ruminants. Whereas palpebral blinking, lacrimation, vocalization, excessive salivation, tachypnea, limb movement are found in light anesthesia (Galatos, 2011).

Basic parameters such as heart rate, respiratory rate, capillary refill time, color ofmucous membrane, temperature should also be monitored (Galatos, 2011; Taylor, 1991). To ensure normal circulation, respiration, body temperature fluid, oxygen and electrolyte, specific drugs etc should be readily available (Galatos, 2011; Taylor, 1991).

Monitoring is essential until recovery for avoiding digestive and respiratory system's complication and only after returning of swallowing, coughing reflexes the endotracheal tube is removed and supported to sternal recumbency in small ruminants (Galatos, 2011; Taylor, 1991). Monitoring apparatus permits for a precise appraisal of anesthetic depth and depression of respiratory, cardiovascular and central nervous system by assessing electrocardiography, arterial hemoglobin oxygen, end-tidal CO2, blood pressure, arterial blood gases and gaseous anesthetic concentration. In absence of monitoring equipment, evaluation of anesthetic depth is tough in small ruminants.

In small ruminants, rotation of the eye is not a practical standard to measure anesthetic depth (Riebold, 2007). During anesthesia, corneal reflex sustains. In both light and deep anesthesia, mydriasis may be found.

Deep anesthesia may be represented when mydriasis is present with non-appearance palpebral reflex and passive ruminal fluid flows continuously. Whereas inadequate anesthesia is indicated by limb, head motion or swallowing activity along with the peristaltic activity of the esophagus (Galatos, 2011).

Normal values of heart rate in small ruminants are 80 to 150 beats/min (Lin and Pugh, 2002). With age heart rates varies and it may decrease with the depth of anesthesia (Riebold, 2007). Increased anesthetic depth is indicated by the decreased pulse pressure found at digital, caudal auricular, radial, and saphenous arteries; however, this method is intuitive (Riebold, 2007).

During anesthesia respiratory rate should be 20-40 breaths/min and the tidal volume may be estimated while using a rebreathing bag (Lin and Pugh, 2002).

Adequate tissue perfusion is suggested by the pink mucus membrane and 1 to 2 seconds of capillary refill time (Riebold, 2007). Pain response should be noted to evaluate anesthetic depth (Riebold, 2007).

For correction of preexisting dehydration, increased cardiac output, replacing intra-operative losses, avoidance of hypotension or to ensure tissue perfusion during prolonged anesthesia, balanced electrolyte solution or lactated ringer solution should be infused intravenously at a rate of 5-10 mL/kg/hour (Riebold, 2007; Ivany and Muir, 2004).

To intercept hypoglycemia, 5% dextrose solution at 2 to 5 mL/kg/hour should be administered to the small ruminants younger than 3 months (Galatos, 2011).

When hematocrit is less than 20% to 25%, a blood transfusion may be necessary (Thurmon and Benson, 1993). In case of consequential blood loss of 20 mL/kg bodyweight, hemoglobin (20 mL/kg bodyweight) or colloids (10-20 mL/kg bodyweight) is recommended (Posner *et al*., 2003). Sodium bicarbonate can be infused in the case of metabolic acidemia (Galatos, 2011).

Although in adult small ruminants hypothermia is rarely found (Riebold, 2007), in young small ruminants hypothermic condition during anesthesia is very common and precaution should be taken to circumvent it (Lin and Pugh, 2002).

During prolonged anesthesia hypoventilation and apnea are very common in small ruminants and oxygen supplementation, assisted or controlled ventilation should be anticipated (Riebold, 2007; Valverde and Doherty, 2008).

Hypotension takes place when mean arterial blood pressure is less than 65 to 70 mm Hg (Hall *et al*., 2001; Ivany and Muir, 2004) and to correct it, the rapid fluid should be provided along with reducing the anesthetic depth (Hall *et al*., 2001).

2.13 Recovery

In comparison to other large animals, such as horses, recovery from anesthesia in ruminants is a very calm process. To allow any material in the throat to exit from the mouth under gravity, the head should be supported at a lower level than the rest of the body when in lateral recumbency. As soon as the patient is in sternal recumbency, its head should be placed low as possible to allow drainage of saliva and gut contents. Until the swallowing reflex returns the endotracheal tube should be retained in place. While removing the tube, the cuff should be partially inflated to ensure no aspiration occurs. The patient is kept in recumbency until it rises and stays standing of its own accord (Hodgkinson and Dawson, 2007). Patients should be allowed to recover in a quiet and comfortable environment. As anesthetized patients thermoregulate poorly, they should be left in a dry and warm place (Carroll and Hartsfield, 1996).

During general anesthesia, sedation, anesthesia, protection of the airway and control of pain in the perioperative period are important contemplation in small ruminants. Although ruminants are classically pondered as food animals, they are used universally in research and teaching and progressively important as companion animals. No matter what their use is, the drugs and techniques for anesthesia and analgesia must be used to ensure their minimal stress and discomfort during the perioperative period.

Chapter 3

Materials and methods

3.1 Study area

The study was conducted at Shahedul Alam Quaderi Teaching Veterinary Hospital (SAQTVH), Chattogram Veterinary and Animal Sciences University (CVASU), Chattogram, Bangladesh.

Figure 1: Geographical location of the study area.

3.2 Study period

The study was conducted from January 2019 to December 2019.

3.3 Study design

The present study was conducted on 20 clinical cases of goats of either sex, aged 6 months to 3 years, and weighing from 10 to 45 kg. The selection of goats for inclusion in the study was based on the requirement for general anesthesia and owner's consent. A preoperative history was obtained and a routine pre-anesthetic physical examination was performed on each goat. The goats were kept off feed for 6hours and water was withheld for 2 hours prior to induction of anesthesia to prevent ruminal tympani during anesthesia. They were not medicated before anesthesia. Anesthesia was carried out in a room temperature controlled at 21 to 25°C.

Schematic diagram of the research program

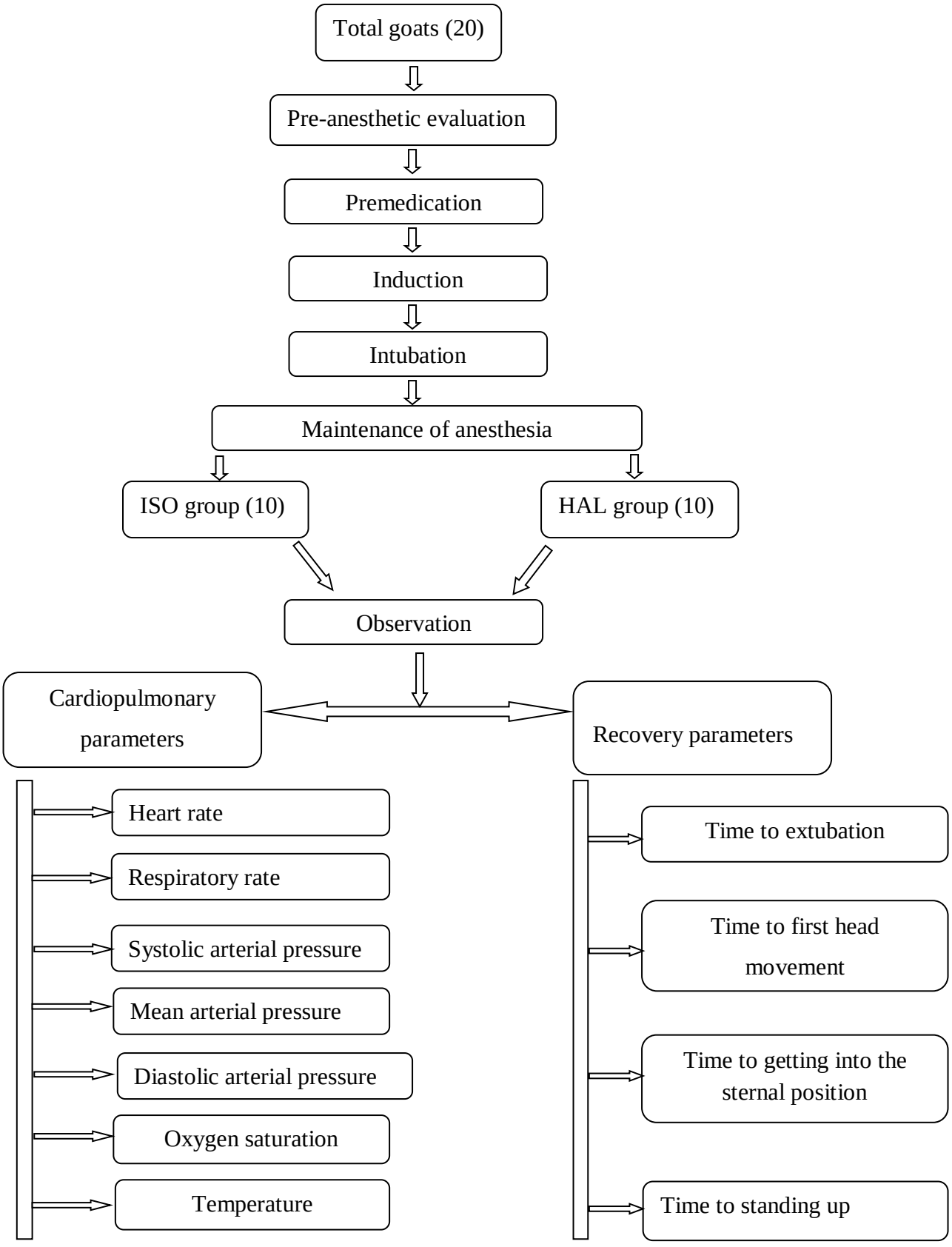

Figure 2: The overall experimental design of this study.

3.4 Anesthetic procedures

All goats presented for various surgical affections requiring general anesthesia (Table 1) were randomly divided into two groups: HAL (n = 10) and ISO (n = 10). Pre-anesthetic values for heart rate (HR), respiration rate (RR), temperature were obtained with the goat resting in a room 15 min before induction of anesthesia.

Table 1. List of Surgical procedures performed in animals of HAL (n=10) and ISO (n=10) groups.

Group	Sex	No of animals	Surgical procedures
HAL	Male	8	Tube cystostomy
	Male	1	Endoscopy
	Female	1	Ear cropping
ISO	Male	9	Tube cystostomy
	Female	1	Intra Medullary Pinning

3.4.1 Premedication

All goats were premedicated with Diazepam (Sedil®, Square Pharmaceuticals Ltd) @ 0.5 mg/kg, intravenously.

3.4.2 Induction

Anesthesia was induced by intravenous infusion of propofol (Pofol®, Popular Pharmaceuticals Ltd.) @ 3mg/kg, intravenously.

Figure 3. Induction of anesthesia.

3.4.3 Intubation

After induction when the eyes had rotated ventrally and medially and the palpebral reflex was abolished, goats were reposed in sternal recumbency for intubation. A loop of gauze around the upper jaw and another loop around the lower jaw and tongue were placed to open the mouth of the goats. The head was lifted up and the head and neck were kept in a straight line for better visualization of the epiglottis and larynx. A laryngoscope was used to depress the base of the tongue and epiglottis for visualization of the larynx. A cuffed endotracheal tube was inserted and the cuff was inflated. Confirmation of proper tube placement was performed by seeing the fogging in the tube and by placing a few strands of gauze at the connector end of the ET tube which blows away with expiration when the tube is correctly placed. The tube was connected to the anesthesia machine. Animals were repositioned in right lateral recumbency after intubation.

Figure 4. Endotracheal intubation in goat.

Figure 5. Confirmation of proper tube placement by blowing of gauze.

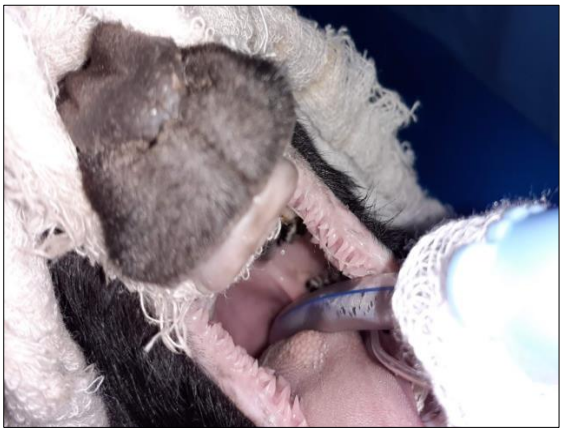

Figure 6. Confirmation of proper tube placement by seeing fogging in tube.

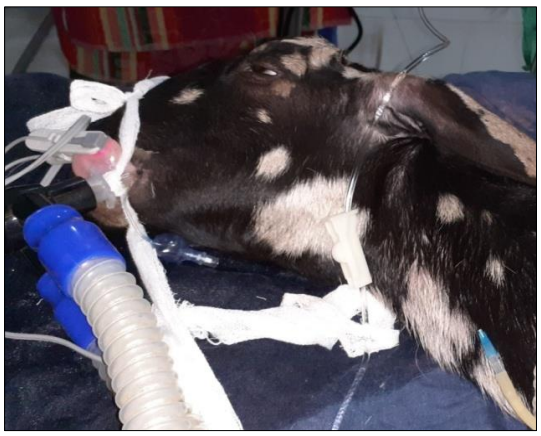

Figure 7. Connection of ET tube with the circuit of anesthesia machine.

3.4.4 Maintenance

Isoflurane (Flurane inhalation®, Techno Drugs Ltd.) @ 1.5-2.5% and Halothane (Halosin®, ACI Ltd) @ 2.5-4% were used for maintenance of anesthesia via a semi-closed rebreathing system. 100% oxygen at a flow rate of 20 ml/kg/min was used.

The vaporizer setting was adjusted according to the depth of anesthesia after monitoring the animal's response to various reflexes and by lack of painful response to surgery. The surgical procedures were completed between 50 and 60 min duration and inhalation anesthesia was maintained up to 60 min in all cases. The endotracheal tube with its cuff inflated was left undisturbed until the return of swallowing reflex (i.e., when the animal started to chew, moved its tongue and retracted it when pulled outwards, showed evidence of the return of good laryngeal control), following which the tube was disconnected from the anesthesia machine and goats were allowed to breathe in room air. The goats were monitored continuously during the recovery period until they were standing individually.

Figure 8. Maintenance of inhalation anesthesia during the surgical procedure.

3.4.5 Fluid and Temperature

Throughout the period of anesthesia, goats were administered intravenous normal saline solution (Normal saline®; The ACME laboratories Ltd) @ 10 ml/kg/hour in both the groups.

A heating pad, a heat and moisture exchange filter was used to maintain normothermia.

3.5 Parameters

All parameters were collected using a vital sign monitor. HR and Electrocardiogram (ECG) were monitored using a multi-functional electrocardiograph via hookup to Einthoven's triangle. SAP, MAP and DAP were measured by a non-invasive oscillometric cuff placed on the right thoracic limb over the radial artery, which was positioned at heart level. Blood oxygen saturation (SpO2) was measured with a pulse oximeter applied to the tongue or the ear. RR was determined by the movement of the rebreathing bag and/or chest movement. All parameters were recorded at the time of breathing circuit connection that was considered as baseline value and 5 min interval after that up to 60 minutes.

Figure 9. Collection of parameters during monitoring of anesthesia.

At the end of the surgery, the vaporizer was closed and 100% O2 was given into the system until the animals woke up. The times at which the goat made the first swallowing attempt the endotracheal tube was then removed. Time to extubation of animals, time to first head movement, time to getting into the sternal position and time to stand up were observed and recorded after discontinuation of the anesthetic. The time of extubation was determined according to the starting of swallowing reflex and jaw movements.

Criteria used to evaluate the quality of induction; anesthesia and recovery in goats were summarized in Table 2.

The extent of salivation/lacrimation was graded as no salivation/lacrimation; mild salivation/ lacrimation; moderate salivation/lacrimation; and profuse salivation/lacrimation. The extent of regurgitation was scored as mild = small amount of ruminal contents present within the oral cavity; severe = extensive volume of rumen contents coming out through mouth or nostrils (Modified from Bodh *et al.*, 2014 and Prassinos *et al.*, 2005).

Table 2. Criteria used to evaluate the quality of induction, anesthesia and recovery in goats induced with propofol and maintained with halothane (n =10) or isoflurane (n=10).

	Response		
Stage	Good	Fair	Poor
Anesthetic induction*	Smooth induction, no sign of excitement, rapid sternal recumbency; easy tracheal intubation	Slightly prolong induction, mild signs of excitement; attempts to arise after resuming recumbency; reflex response to tracheal intubation	Signs of excitement; attempts to stands, inability to tracheal intubation.
Anesthesia**	No response to surgical stimulation	Mild response to surgical stimulation	Very responsive to surgical stimulation (gross purposeful movement, such as lifting head, chewing, and vocalization)
Recovery*	Smooth, satisfactory, resumes sternal position, stands in a reasonable amount of time and is able to walk with minimal ataxia	some struggling, transient excitement, some instability when standing	Unsatisfactory, Circling, premature attempts to stand, prolonged struggling

*Modified from Carroll *et al*., 1998 and Prassions *et al*., 2005.
**Modified from Lin *et al*., 1997

3.6 Statistical analyses

Data obtained from the study were stored in an MS excel spreadsheet and exported to Stata-IC-13 (Stata Corp, 4905, Lakeway Drive, college station, Texas, USA), for conducting statistical analysis. The results were expressed as means$\pm$ SD. Analysis of variance (ANOVA) was used to compare the means at different time intervals among the two groups. To compare the mean values at different intervals with their base values in each group, a paired "t" test was used. $p < 0.05$ and $p < 0.01$ values were considered significant.

Chapter 4

Result

4.1 Findings of the heart rate (HR):

All data were expressed as mean ± SD. A significant decrease in heart rate was found in the HAL group when compared to the base-line value that was immediately after connecting the circuit to patients (Figure 10). Statistically significant ($p<0.05$) differences in heart rate were found between the two groups (Figure 10).

4.2 Findings of the respiratory rate (RR):

There was no significant difference between HAL and the ISO group in respiratory rate (Figure 11).

In the HAL group, a significant difference ($p<0.05$) was found in 60 minutes in comparison to the base value (Figure 11).

4.3 Findings of the oxygen saturation (SpO_2):

No significant differences in SpO_2 were found between the two groups or from base value to other values (Figure 12).

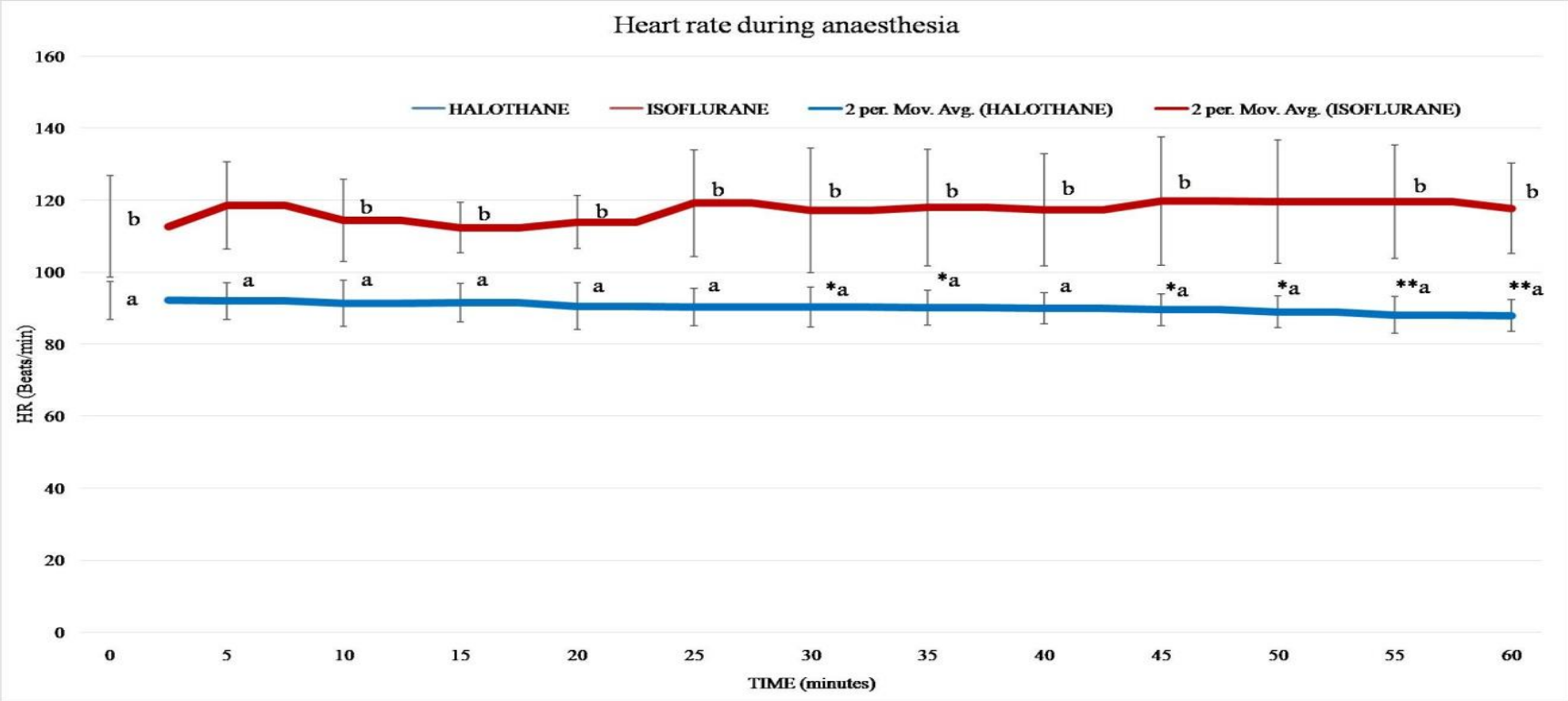

Figure 10. Values of heart rate (HR) in small ruminants during halothane and isoflurane maintenance anesthesia. Each point and vertical bar represents the mean ± S.D. (n=10).

*: Differs significantly ($p<0.05$) from base value.

**: Differs significantly ($p<0.01$) from base value.

[a, b]: Differs significantly ($p< 0.05$) between the two groups at corresponding intervals.

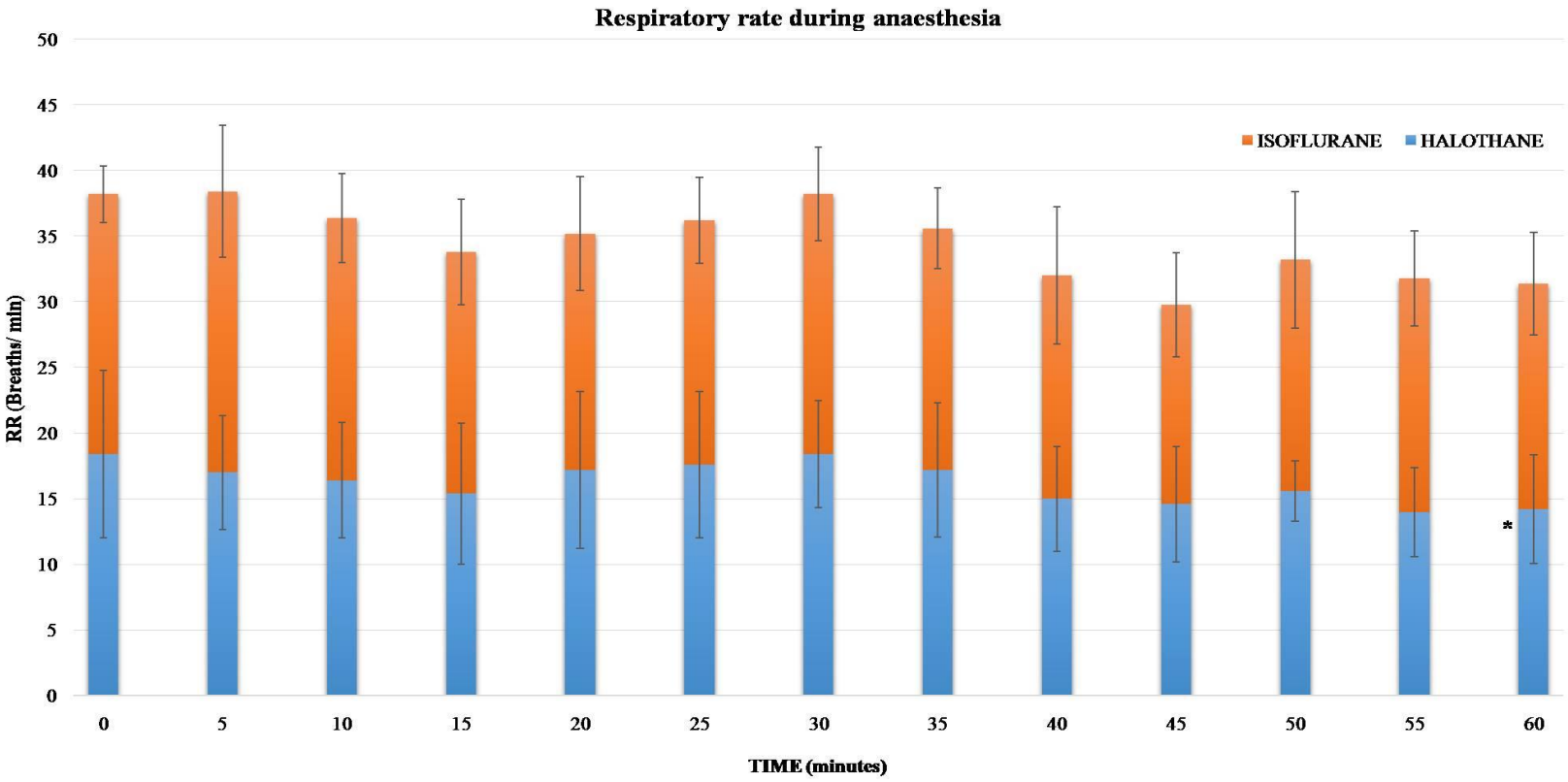

Figure 11. Values of respiratory rate (RR) in small ruminants during halothane and isoflurane maintenance anesthesia. Each column represents the mean value with a vertical bar indicating S.D. (n=10).

*: Differs significantly ($p<0.05$) from base value.

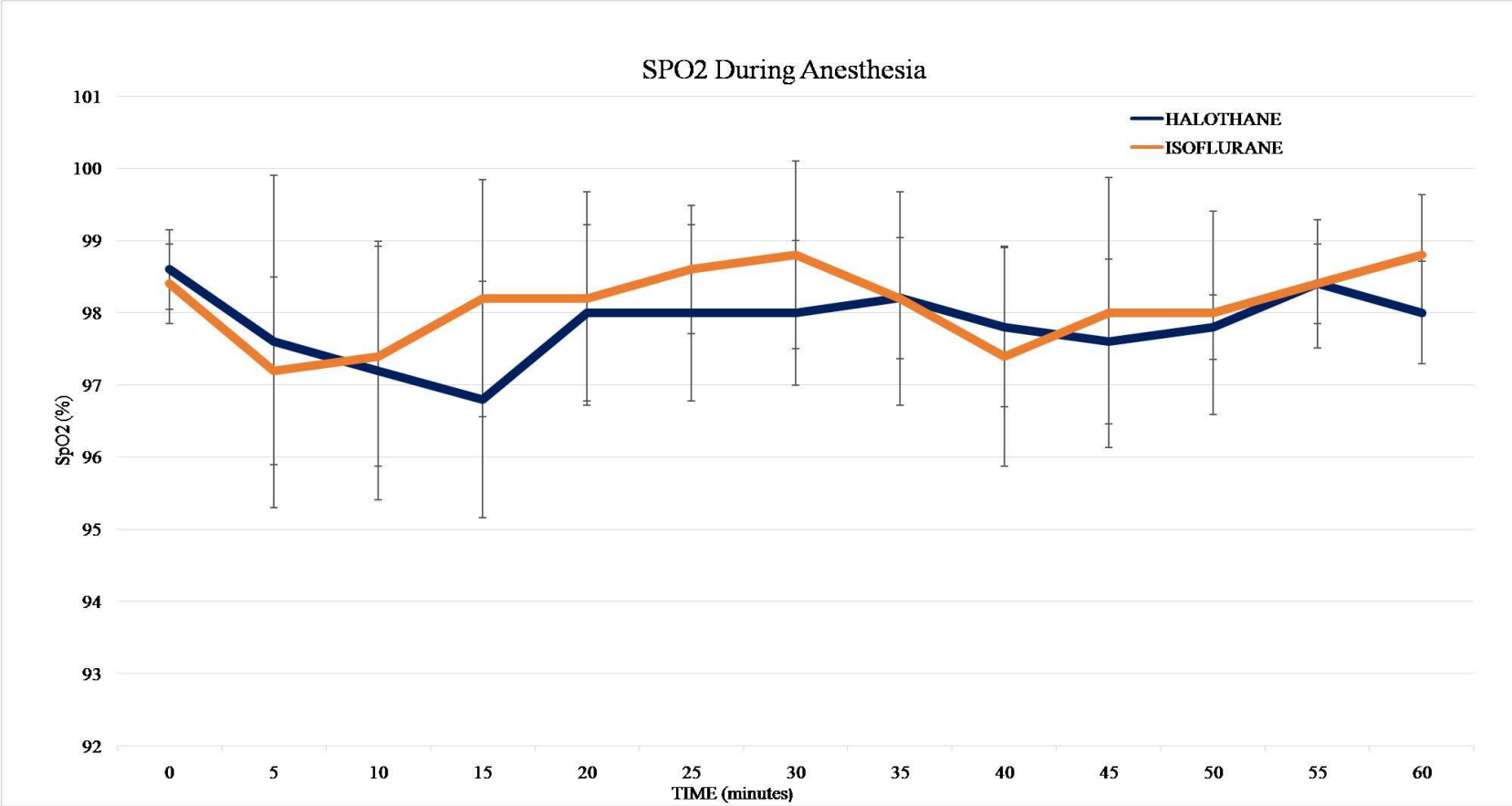

Figure 12. Values of Oxygen saturation (SpO2) in small ruminants during halothane and isoflurane maintenance anesthesia. Each point and vertical bar represents the mean ± S.D (n=10). No significant differences were found in between two groups or from base value to other values.

4.4 Findings of the blood pressure

The systolic arterial pressure decreased significantly ($p<0.05$) in the HAL group from ten minutes to twenty-five minutes (Figure 13) where there was no significant differences in the ISO group with the base value. SAP differed significantly ($P<0.05$) between the two groups (Figure 13).

In case of DAP, a significant difference ($p<0.05$) was found at twenty-five minutes from base value in the HAL group (Figure 14). There were significant differences ($p<0.05$) of DAP in between the two groups (Figure 14).

Similarly, in case of MAP, significant differences ($p<0.05$) were found only in HAL group at twenty-five and thirty-five minutes (Figure 15) from base value. MAP also differs significantly between the HAL and the ISO groups from five to fifty minutes except in forty-five minutes (Figure 15).

4.5 Findings of Temperature

Significant decreased from base value in rectal temperature during anesthesia maintenance were found in both HAL and ISO groups (Figure 16). At 45 and 50 minutes of anesthesia, significant temperature differences were seen between HAL and ISO groups (Figure 16).

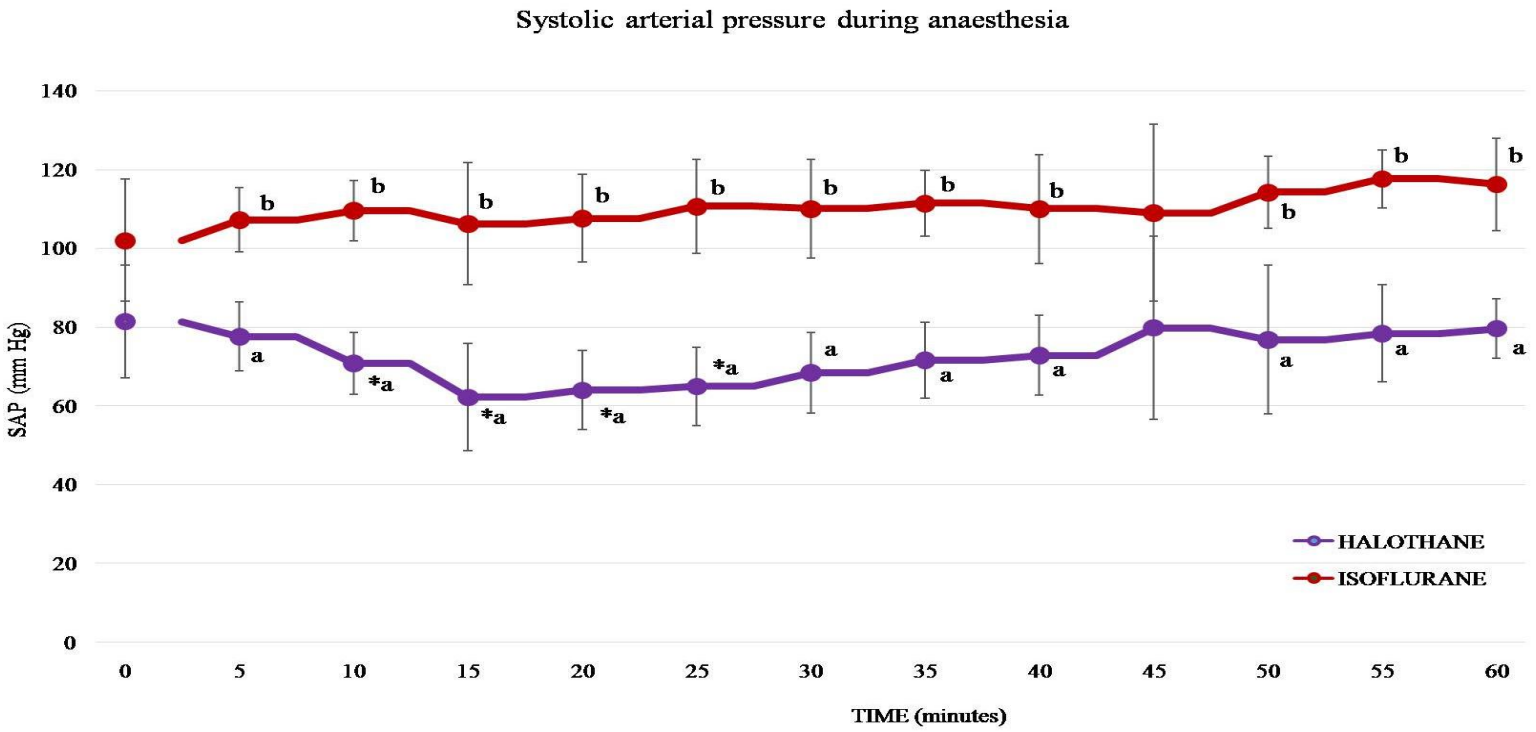

Figure 13. Values of Systolic arterial pressure (SAP) in small ruminants during halothane and isoflurane maintenance anesthesia. Each point and vertical bar represents the mean ± S.D. (n=10).

*: Differs significantly ($p<0.05$) from base value.

[a, b]: Differs significantly ($p< 0.05$) between the two groups at corresponding intervals.

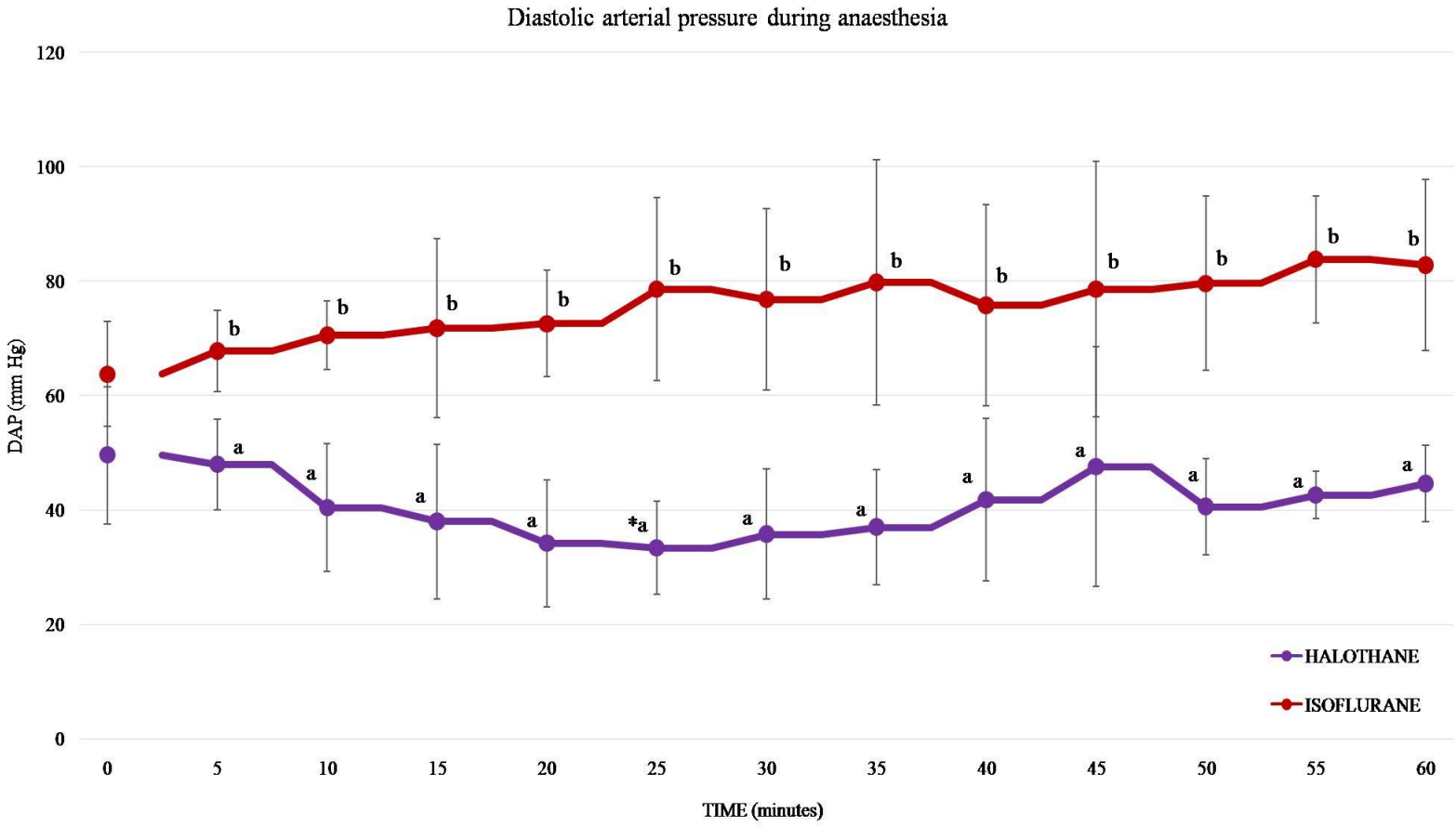

Figure 14. Values of Diastolic arterial pressure (DAP) in small ruminants during halothane and isoflurane maintenance anesthesia. Each point and vertical bar represents the mean ± S.D. (n=10).

*: Differs significantly ($p<0.05$) from base value.

[a, b]: Differs significantly ($p< 0.05$) between the two groups at corresponding intervals.

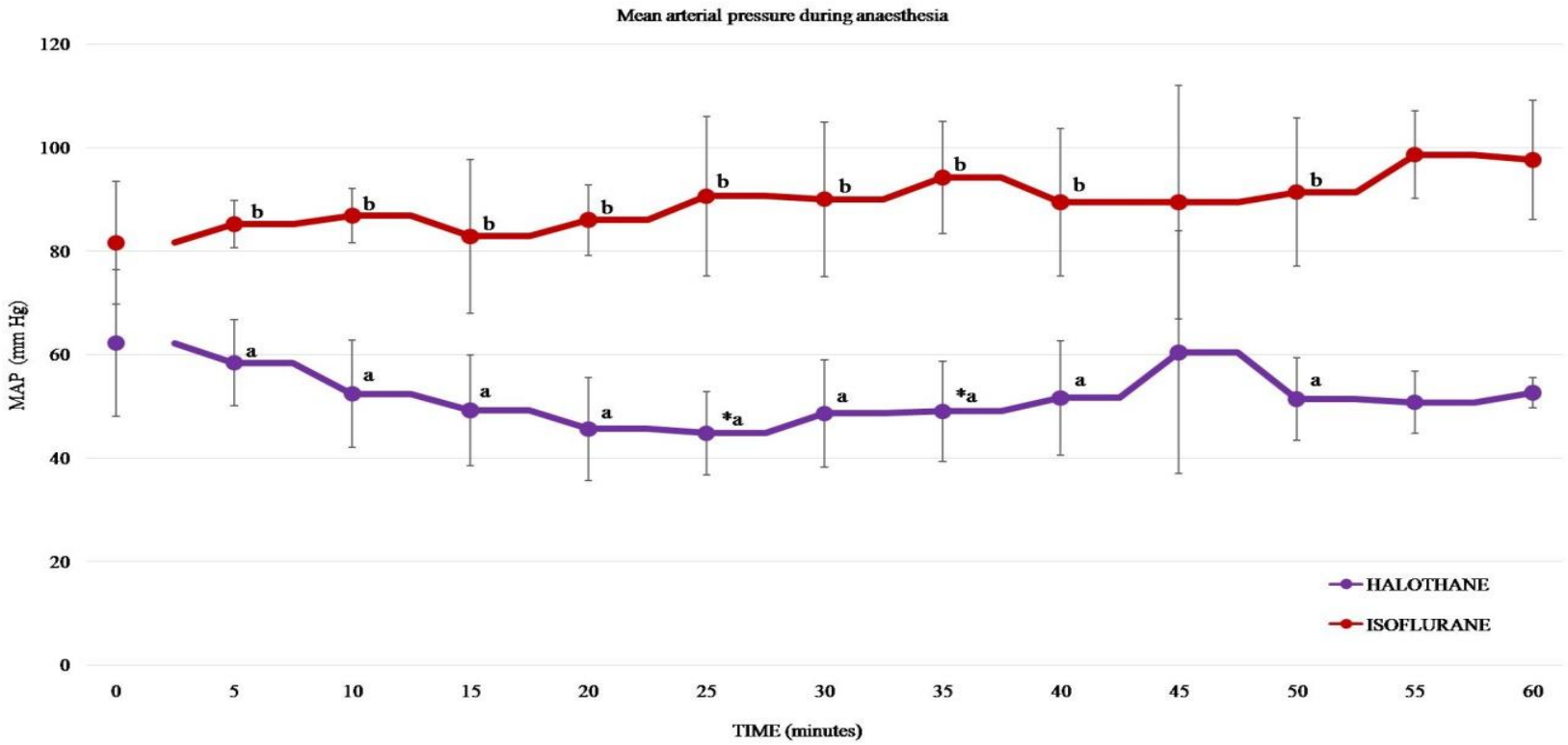

Figure 15. Values of Mean arterial pressure (MAP) in small ruminants during halothane and isoflurane maintenance anesthesia. Each column represents the mean value with a vertical bar indicating S.D. (n=10).

*: Differs significantly ($p<0.05$) from base value.

[a, b]: Differs significantly ($p< 0.05$) between the two groups at corresponding intervals.

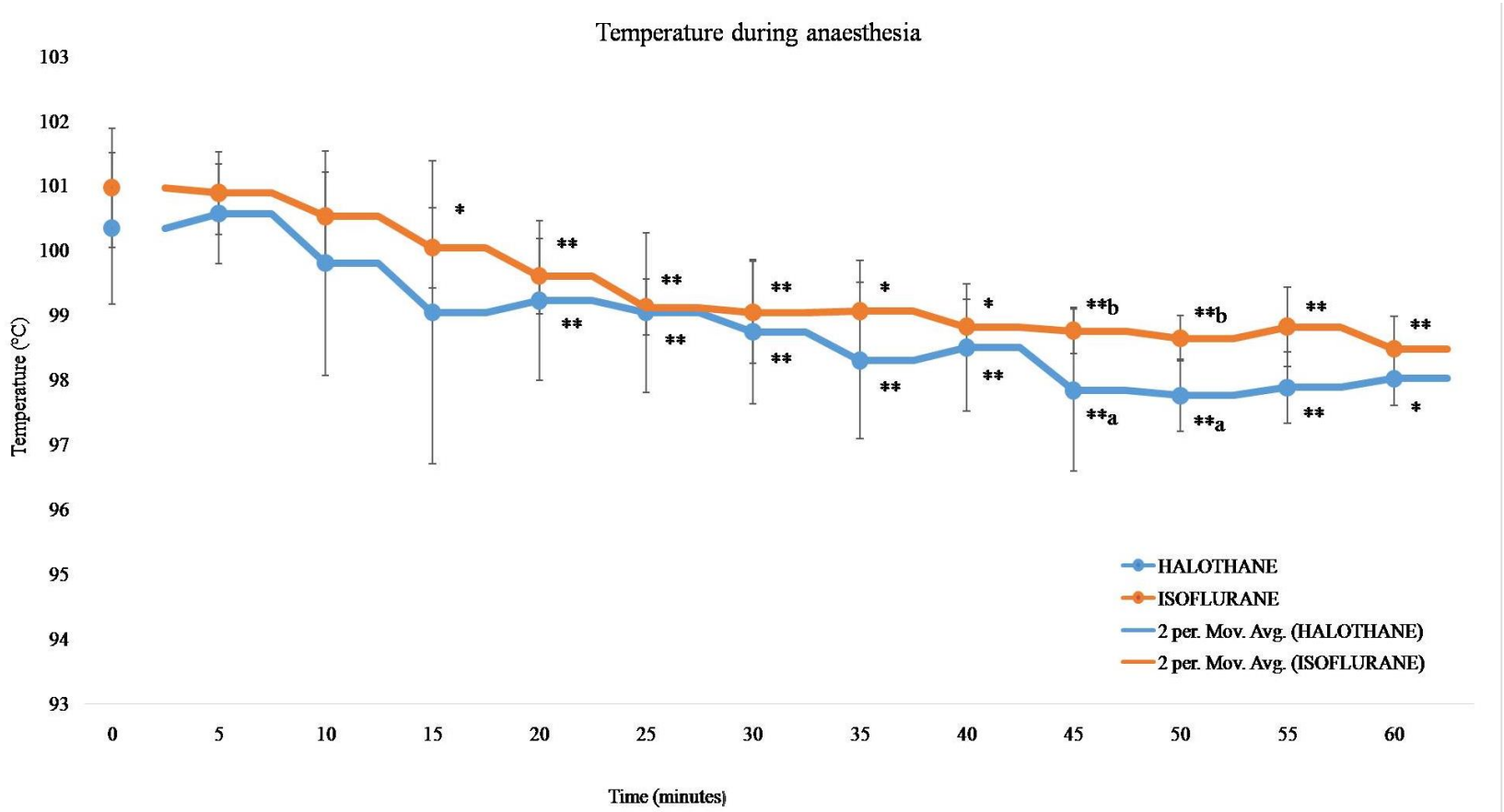

Figure 16. Values of Temperature in small ruminants during halothane and isoflurane maintenance anesthesia. Each point and vertical bar represents the mean ± S.D. (n=10).

*: Differs significantly ($p<0.05$) from base value.

**: Differs significantly ($p<0.01$) from base value.

[a, b]: Differs significantly ($p< 0.05$) between the two groups at corresponding intervals.

4.6 Recovery findings

In the ISO group, recovery was faster in compare to the HAL group. Time to extubation, time to regain thoracic recumbency and time to stand up were significantly ($p<0.05$) lesser in the ISO group compared to the HAL group (Figure 17). No significant difference was observed in head movement between the two groups (Figure 17).

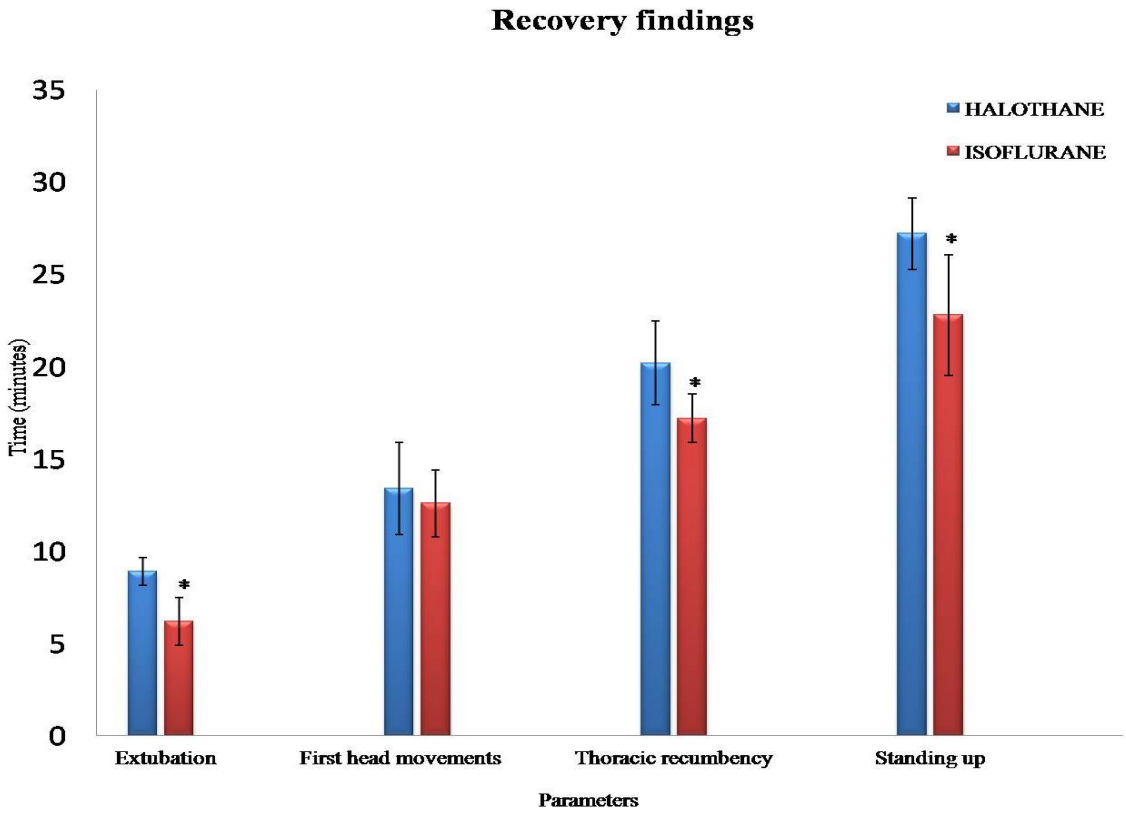

Figure 17. Recovery data comparing halothane (HAL) Vs. isoflurane (Iso) in small ruminants. Each column represents the mean value with a vertical bar indicating S.D. (n=10).

*: Significant difference between the anesthesia agents ($P < 0.05$).

In case of isoflurane maintenance anesthesia, recovery was smoother with good standing coordination. Mild regurgitation was found in two goats in the HAL group and one goat in the ISO group (Table 3).

In the HAL group, mild salivation was observed in three goats and moderate salivation was found in two goats (Table 3). On the other hand, mild salivation was found in two goats and no salivation was found in eight goats of the ISO group (Table 3).

No lacrimation was found in either of the two groups. Evanescent shivering and incoordination of the limb were found in three goats during recovery from halothane maintenance anesthesia. In the HAL group, post-anesthetic shivering was observed in three goats (Table 3).

Table 3. Summary of induction and recovery quality, and occurrence of side effects in goats induced with propofol, maintained with halothane and isoflurane.

	HAL (n=10)	ISO (n=10)
Quality of induction	Good (10)	Good (10)
Quality of anesthesia	Good (10)	Good (10)
Quality of recovery	Good (8), Fair (2)	Good (10)
Regurgitation	Mild (2) No regurgitation (8)	Mild (1) No regurgitation (9)
Hypersalivation	No salivation (5) Mild salivation (3) Moderate salivation (2)	No Salivation (8) Mild salivation (2)
Lacrimation	No Lacrimation (10)	No Lacrimation(10)
Post-anaesthetic shivering	Shivering (3) Not observed(7)	Not observed (10)
Post-recovery limb in coordination	Observed (3) Not observed (7)	Not observed (10)

Numbers in parentheses denote the number of animals that showed respective signs.

Chapter 5

Discussion

Halothane (HAL) and isoflurane (ISO) have long been used as inhalation anesthesia in the clinical practices of veterinary medicine (Mutoh *et al.*, 1997). Dose-dependent cardiopulmonary depression is induced by inhalation anesthesia in all animals (Polish *et al*., 2001). Halogenated anesthetics, like halothane and isoflurane can make alterations to cardiac rate and rhythm (Nakaigawa *et al*., 1995).

In this study, significant differences ($p < 0.05$) in heart rate between HAL and ISO groups were found during the maintenance of anesthesia. For different species or ages, various responses of heart rate during halothane and isoflurane anesthesia have been recorded. In dogs (Frink *et al.*, 1992), horses (Steffy *et al*., 1987) and bulls (Greene *et al*., 1998) increased heart rate was observed. Whereas, decreased heart rate were observed in lambs (Brett *et al*., 1987) and piglets (Schieber *et al*., 1986). Constant or increased heart rate is caused by an increased alveolar concentration of inhalation anesthetic in the dog (Steffeyand Howland, 1979) and decreased heart rate is caused by the increased vagal tone that increases anesthetic depth (Hall and Clarke, 1983). In our study decreased heart rate in HAL group was associated with an increase in anesthetic depth. Halothane produces dose-dependent depression of the cardiovascular system and decreases arterial blood pressure (Steffey and Mama, 2007). Isoflurane has been reported to produce less myocardial depression (Merin *et al*., 1991). In the ISO group, the non-significant ($p > 0.01$) increase in heart rate was in conflict with the results of previous studies in cats (Hikasa *et al*., 1997) and goats (Hikasa *et al*. 1998). But similar increased heart rate during isoflurane maintenance anesthesia was found in water buffalo (Bodh *et al*., 2014). The increased heart rate of ISO group in our study may be due to an inadequate level of anesthesia or for decreased peripheral resistance or due to differences in the amount of sympathetic stimulation within the two groups (Bodh *et al*., 2014). As isoflurane does not reduce heart rate, it is more advantageous than halothane for maintaining sufficient cardiac output during anesthetic conditions in small ruminants.

During halothane anesthesia decreased respiratory rate and depth were observed in bulls (Greene *et al*., 1998) and cattle (Takase, 1976). In our study, the respiratory rate decreased significantly ($p<0.05$) for a very short duration in HAL group. In halothane maintenance anesthesia respiratory depression may be observed due to simultaneous administration of halothane with oxygen and hypotension that might have caused increased physiological dead space (Hull and Reilly, 1968). Halothane may depress ventilation by depressing respiratory centers in central nervous system, by suppressing the function of motor neurons, diaphragm and intercostals muscles, by diminishing peripheral drive from the chemoreceptors at the carotid bodies and also by the loss of wakefulness drive that is behavioral control (Knill and Clement, 1984; Knill and Clement, 1985). In case of ruminants, lateral recumbency and continuous ruminal fermentation causing bloat during anesthesia produce impaired ventilation (Fujimoto and Lenehan, 1985; Lin *et al*., 2012). In our present study, no significant difference in RR between the two anesthetics was observed. It might be due to preoperative fasting that caused less fermentation and bloat and also for governing oxygen along with anesthesia that prevented hypercarbia.

The SpO_2 concentration for halothane and isoflurane were within normal reference ranges. Administration of 100% oxygen along with inhalation anesthetics in both groups might have led to higher values of SpO_2 observed in the present study.

During halothane anesthesia, hypotensive effect in cattle (Hall, 1957; Wolf *et al*., 1968) and buffalo (Bose and Kohli, 1983; Gahlawat *et al*., 1986) was reported. In this present study, significant ($p<0.05$) decreased in SAP, DAP and MAP were found in HAL group. SAP, DAP and MAP also differed significantly between two groups. In HAL group the decreased arterial blood pressure may be caused by depression of myocardial contractility and decreased cardiac output during halothane anesthesia (Stoelting, 1991). Although halothane induces a dose-dependent decrease in arterial blood pressure and cardiac output, it affects very little on total peripheral resistance in dogs (Steffey and Howland, 1978) and goats (Hikasa *et al*., 1998). On the contrary, isoflurane is reported to produce a greater fall in peripheral vascular resistance with decreased arterial blood pressure and

little decreased cardiac output in dogs and cats (Steffey *et al*., 1987; Bernard *et al*., 1990) and goats (Hikasa *et al*., 1998).

Although the body temperature was within physical limits, the rectal temperature decreased significantly in both anesthetic groups. The drop of temperature in ISO group was lower than HAL group at 45 and 50 minutes. In HAL group severe heat loss or hypothermia might be caused by vasodilatation (Jones and McLaren, 1965). In a study in humans, greater decrease in body temperature was found in the halothane group than the isoflurane group, which is similar to our study (Ramachandra *et al*., 1989). In addition, during halothane anesthesia in adult water buffaloes significant decrease in rectal temperature was reported (Malik, 2008). The decrease in rectal temperature in both the groups might be due to decreased skeletal muscle tone, reduced metabolic rate, and muscle relaxation along with depressed thermoregulatory center (Matsukawa *et al*., 1995).

Hypothermia in HAL group might be one of the causes for delayed recovery in this group. Due to hypothermia, the blood/gas solubility of inhalant anesthetics is increased and it causes slow saturation in the blood and tissues and slow induction and recovery (Dohoo, 1990). Rapid recovery in the ISO group than the HAL group might also be caused by relative insolubility; faster changes in alveolar concentration and lower blood-gas partition coefficient during isoflurane anesthesia. These findings support the similar reports in horses (Matthews *et al*., 1992 and Whitehair *et al*., 1993) and water buffalo (Bodh, 2014). The early recovery of isoflurane anesthesia attributes to less stress response, better cardiovascular function, fewer changes in hepatic circulation and quicker elimination of anesthetics (Riazuddin *et al*., 2004). Whereas slower recovery in halothane maintenance anesthesia might be caused by increased stress that leads to catabolic pathways and depletes energy sources (Wagner *et al*., 1991).

During general anesthesia in ruminants, regurgitation is the most common complication (Reid *et al*., 1993). In the light plane of anesthesia, regurgitation occurs due to active but uncontrolled reflex mechanism that passes the ruminal ingesta up the esophagus into the pharynx. Whereas deep anesthesia regurgitation occurs through a passive process of

increasing intra-ruminal pressure unanimous by poor esophageal or eso-pharyngeal sphincter tone (Bodh *et al*., 2014). The risk of regurgitation increases in case of inadequate fasting and improper positioning of patients where ruminal contents submerge the esophageal opening and prevents gas eructation from rumen that leads to distension of rumen and regurgitation of ruminal contents (Bodh *et al*., 2014).

To facilitate drainage of saliva and ruminal contents from the mouth and to prevent airway blockage in a deep plane of anesthesia, the patients were restrained in head-down position in lateral recumbency. Moderate salivation in the HAL group and mild salivation in both HAL and ISO group were observed in this study. This might be caused by decreased swallowing reflex (Kokkonen and Eriksson, 1987) or for remaining partially open jaws due to endotracheal tube placement (Bodh *et al*., 2014).

The deep plane of surgical anesthesia and lack of parasympathetic stimulation might have attributed to no lacrimation observed during maintenance of anesthesia in both HAL and ISO groups in this study.

In the HAL group, post-anesthetic shivering observed in three patients might be due to central nervous stimulated residual excitatory effect (Auer *et al*., 1978) or due to hypothermia found in the HAL group during recovery. Core temperature at the end of surgery is the most important clue to determining the factor in the occurrence of post-operative shivering (Lienhar *et al*., 1992). This supports the thermoregulatory shivering in HAL group due to post-operative hypothermia in this study.

The findings of the present study indicate isoflurane produces less cardiovascular depression than halothane with faster recovery. According to our knowledge no research was conducted on general anesthesia maintained with gaseous anesthetics incase of ruminants in Bangladesh. The present study was undertaken to evaluate the effects of halothane and isoflurane anesthetics in small ruminants. A limitation of this study includes small a sample size which does not represent the whole population due to a short period of study.

Chapter 6

Conclusion

From the results of the present study, it is concluded that general anesthesia maintained with isoflurane in propofol-induced anesthesia in small ruminants resulted in less suppressive effects on the cardiovascular system compared to halothane maintenance anesthesia. Recovery time in case of halothane anesthesia was 27.2±1.92, whereas in isoflurane it was 22.8±3.27 minute. This proves shorter recovery time from isoflurane anesthesia than halothane. Also, isoflurane anesthesia found to provide better recovery quality with minimum side effects like regurgitation, hypersalivation etc than halothane anesthesia. All these findings suggest that isoflurane maintenance anesthesia is more advantageous than anesthesia maintained with halothane in small ruminants that supports previous researches. Inhalation anesthesia plays a vital role in the easy and better handling of small ruminants. Though halothane and isoflurane both can be used in small ruminants, Isoflurane is suggested for the compromised patients.

Recommendations

The outlook towards small ruminants is changing day by day in Bangladesh from food animals to pet animals and laboratory animals for various research purposes. During prolonged surgery of these animals, anesthesia and analgesia are the main concern as like as canine, feline or equine patients. A significant conclusion was found in our present study, although large-sized population would provide the more specified result for a better conclusion. Further research can be executed with a larger sample size in various species of ruminants for more precise findings.

References

Abrahamsen, E.J., 2008. Ruminant field anesthesia. Veterinary Clinics of North America: Food Animal Practice, 24(3):429-441.

Algotsson, L., Messeter, K., Rosen, I. and Holmin, T., 1992.Effects of nitrous oxide on cerebral haemodynamics and metabolism during isoflurane anaesthesia in man. Acta anaesthesiologica scandinavica, 36(1):46-52.

Alibhai H. I. K., Clarke K. W., Hughes G. 1994. Minimum alveolar concentration (MAC) in goats. Proceedings of the 5th International Congress of Veterinary Anesthesia, Guelph. Abstract Book, p 87.

Antognini, J.F. and Eisele, P.H., 1993. Anesthetic potency and cardiopulmonary effects of enflurane, halothane, and isoflurane in goats. Laboratory animal science, 43(6):607-610.

Bernard, J.M., Wouters, P.F., Doursout, M.F., Florence, B., Chelly, J.E. and Merin, R.G., 1990. Effects of sevoflurane and isoflurane on cardiac and coronary dynamics in chronically instrumented dogs. Anesthesiology: The Journal of the American Society of Anesthesiologists, 72(4):659-662.

Bettschart-Wolfensberger, R., Semder, A., Alibhai, H., Demuth, D., ShojaeeAliabadi, F. and Clarke, K.W., 2000. Cardiopulmonary side-effects and pharmacokinetics of an emulsion of propofol (Disoprivan®) in comparison to propofol solved in polysorbate 80 in goats. Journal of Veterinary Medicine Series A, 47(6):341-350.

Blaze, C.A., LeBlanc, P.H. and Robinson, N.E., 1988. Effect of withholding feed on ventilation and the incidence of regurgitation during halothane anesthesia of adult cattle. American journal of veterinary research, 49(12):2126-2129.

Bodh, D., Singh, K., Gopinathan, A., Mohindroo, J. and Saini, N.S., 2014. Comparative evaluation of halothane and isoflurane maintenance anesthesia in water buffaloes (Bubalusbubalis). Journal of Applied Animal Research, 42(3):269-277.

Bose, A.S. and Kohli, R.N., 1983. Studies on halothane anaesthesia in buffaloes with special reference to thoracic surgery. Indian journal of veterinary surgery. 4:50-57.

Brett, C.M., Teitel, D.F., Heymann, M.A. and Rudolph, A.M., 1987. The Cardiovascular Effects of Isofiurane in Lambs. Anesthesiology: The Journal of the American Society of Anesthesiologists, 67(1):60-65.

Bunker, J.P., 1968. Final report of the national halothane study. Anesthesiology: The Journal of the American Society of Anesthesiologists, 29(2):231-232.

Bunker, J.P., Forrest, W.H., Mosteller, F., Vandam, L. D., 1969. A study of the possible association between halothane anesthesia and post-operative hepatic necrosis; report. The National Academies Press. P. 179.

Campagna, J.A., Miller, K.W. and Forman, S.A., 2003. Mechanisms of actions of inhaled anesthetics. New England Journal of Medicine, 348(21):2110-2124.

Cantalapiedra, A.G., Villanueva, B. and Pereira, J.L., 2000. Anaesthetic potency of isoflurane in cattle: determination of the minimum alveolar concentration. Veterinary Anaesthesia and Analgesia, 27(1):22-26.

Carroll, G.L. and Hartsfield, S.M., 1996. General anesthetic techniques in ruminants. Veterinary Clinics of North America: Food Animal Practice, 12(3):627-661.

Carroll, G.L., Hooper, R.N., Slater, M.R., Hartsfield, S.M. and Matthews, N.S., 1998. Detomidine-butorphanol-propofol for carotid artery translocation and castration or ovariectomy in goats. Veterinary Surgery, 27(1):.75-82.

Caulkett, N., 2003. Anaesthesia of ruminants. Large Animal Veterinary Rounds, 3(2), pp.1-6.

Correia, D., Nolan, A.M. and Reid, J., 1996. Pharmacokinetics of propofol infusions, either alone or with ketamine, in sheep premedicated with acepromazine and papaveretum. Research in veterinary science, 60(3):213-217.

Dohoo, S.E., 1990. Isoflurane as an inhalational anesthetic agent in clinical practice. The Canadian Veterinary Journal, 31(12):847-850.

Dunlop, C.I., Steffey, E.P., Miller, M.F. and Woliner, M.J., 1987. Temporal effects of halothane and isoflurane in laterally recumbent ventilated male horses. American journal of veterinary research, 48(8):1250-1255.

Dzikiti, B.T., Stegmann, F.G., Dzikiti, L.N. and Hellebrekers, L.J., 2010. Total intravenous anaesthesia (TIVA) with propofol-fentanyl and propofol-midazolam

combinations in spontaneously-breathing goats. Veterinary anaesthesia and analgesia, 37(6):519-525.

Dzikiti, T. B., 2013. Intravenous anaesthesia in goats: a review. Journal of the South African Veterinary Association, 84(1):1-8.

Dzikiti, T.B., Stegmann, G.F., Hellebrekers, L.J., Auer, R.E. and Dzikiti, L.N., 2009. Sedative and cardiopulmonary effects of acepromazine, midazolam, butorphanol, acepromazine-butorphanol and midazolam-butorphanol on propofolanaesthesia in goats. Journal of the South African Veterinary Association, 80(1):10-16.

Eger, E.I., 1981. Isoflurane A Review. Anesthesiology: The Journal of the American Society of Anesthesiologists, 55(5):559-576.

Eger, E.I., Smith, N.T., Stoelting, R.K., Cullen, D.I., Kodis, L.B. and Whitcher, C.E., 1970. Cardiovascular effects of halothane in man. Anesthesiology: The Journal of the American Society of Anesthesiologists, 32(5):396-408.

Elliott, R.H. and Strunin, L., 1993. Hepatotoxicity of volatile anaesthetic agents. British Journal of Anaesthesia, 71(4):611-612.

Ewing, K.K., 1990. Anesthesia techniques in sheep and goats. Veterinary Clinics of North America: Food Animal Practice, 6(3):759-778.

Frink, E.J., Morgan, S.E., Coetzee, A., Conzen, P.F. and Brown, B.R., 1992. The effects of sevoflurane, halothane, enflurane, and isoflurane on hepatic blood flow and oxygenation in chronically instrumented greyhound dogs. Anesthesiology: The Journal of the American Society of Anesthesiologists, 76(1):85-90.

Fujimoto, J.I. and Lenehan, T.M., 1985. The Influence of Body Position on the Blood Gas and Acid-base Status of Halothane-anesithetized Sheep. Veterinary surgery, 14(2):169-172.

Fulton, L.K., Clarke, M.S. and Farris Jr, H.E., 1994. The goat as a model for biomedical research and teaching. Institute for Laboratory Animal Research, 36(2):21-29.

Furtado, K.S. and Andrade, F.O., 2013. Comparison of the beneficial and adverse effects of inhaled and injectable anaesthetics: A mini-review. OA Anaesthetics, 1(2):20-25.

Gahlawat, J.S., Singh, A.P., Peshin, P.K. and Singh, J., 1986. Evaluation of halothane anaesthesia with and without thiopental sodium induction in spontaneously ventilating buffalo calves (Bubalusbubalis). Archiv fur experimentelle Veterinarmedizin, 40(6):862-869.

Galatos, A.D., 2011. Anesthesia and analgesia in sheep and goats. Veterinary Clinics of North America: Food Animal Practice, 27(1):47-59.

Ghurashi, M.A.H., Seri, H.I., Bakheit, A.H., Ashwag, E.A.M. and Abakar, J.A., 2009. Evaluation of ketamine/diazepam anaesthesia for performing surgery in desert goats under field condition. Australian journal of basic and applied sciences, 3(2):455-459.

Gibson, T.J., Johnson, C.B., Murrell, J.C., Hulls, C.M., Mitchinson, S.L., Stafford, K.J., Johnstone, A.C. and Mellor, D.J., 2009. Electroencephalographic responses of halothane-anaesthetised calves to slaughter by ventral-neck incision without prior stunning. New Zealand Veterinary Journal, 57(2):77-83.

Glowaski, M.M. and Wetmore, L.A., 1999. Propofol: application in veterinary sedation and anesthesia. Clinical Techniques in Small Animal Practice, 14(1):1-9.

Gray, P.R. and McDonell, W.N., 1986. Anesthesia in goats and sheep. 2. General-anesthesia. Compendium on Continuing Education for the Practicing Veterinarian, 8(3):127-S135.

Gray, P.R. and McDonnell, W.N., 1986. Anesthesia in goats and sheep. I. Local analgesia. The Compendium on continuing education for the practicing veterinarian (USA).8:S33–39.

Greene, S.A., Tyner, C.L., Morris, D.L. and Hartsfield, S.M., 1988. Comparison of cardiopulmonary effects of isoflurane and halothane after atropine-guaifenesin-thiamylal anesthesia for rumenotomy in steers. American journal of veterinary research, 49(11):1891-1893.

Hall, L. W., Clarke, K. W., 1983. Veterinary anaesthesia. London: BailliereTindall; pp. 104–106.

Hall, L. W., Clarke, K. W., Trim, C. M., 2001. Anaesthesia of sheep, goats and other herbivores. In: Veterinary anaesthesia. 10th edition. London: WB Saunders. pp. 341–366.

Hall, L. W., Clarke, K. W., and Trim, C. M. 2014. General pharmacology of the inhalation anaesthetics. In: Veterinary anaesthesia. 11th edition. London: WB Saunders. pp. 155-168.

Hall, L.W., 1957. Bromochlorotrifluoroethane ("Fluothane"): a new volatile anaesthetic agent. Veterinary Record, 69:615-618.

Handel, I. G., Weaver, B. M. Q., Staddon G. E., Cruz Madorran J. I., 1991. Observation on the pharmacokinetics of propofol in sheep. In: Proceedings of the Fourth International Congress of Veterinary Anesthesia, Utrecht. pp. 143–154.

Hellebrekers, L.J., 1986. Comparison of isoflurane and halothane as inhalation anaesthetics in the dog. Veterinary Quarterly, 8(3):183-188.

Hikasa, Y., Hokushin, S., Takase, K. and Ogasawara, S., 2002. Cardiopulmonary, hematological, serum biochemical and behavioral effects of sevoflurane compared with isoflurane or halothane in spontaneously ventilating goats. Small Ruminant Research, 43(2):167-178.

Hikasa, Y., Okuyama, K., Kakuta, T., Takase, K. and Ogasawara, S., 1998. Anesthetic potency and cardiopulmonary effects of sevoflurane in goats: comparison with isoflurane and halothane. Canadian Journal of Veterinary Research, 62(4):299-306.

Hikasa, Y., Saito, K., Takase, K. and Ogasawara, S., 2000. Clinical, cardiopulmonary, hematological and serum biochemical effects of sevoflurane and isoflurane anesthesia in oxygen under spontaneous breathing in sheep. Small Ruminant Research, 36(3):.241-249.

Hikasa, Y., Yoshikai, T., Takase, K. and Ogasawara, S., 1997. Comparisons of prolonged sevoflurane, isoflurane, and halothane anaesthesia combined with nitrous oxide in spontaneously breathing cats. Journal of Veterinary Medicine Series A, 44(1-10):427-442.

Hodgkinson, O. and Dawson, L., 2007. Practical anaesthesia and analgesia in sheep, goats and calves. In Practice, 29(10):596-603.

Hoffman, W.E., Charbel, F.T., Edelman, G., Albrecht, R.F. and Ausman, J.I., 1995. Nitrous oxide added to isoflurane increases brain artery blood flow and low frequency brain electrical activity. Journal of neurosurgical anesthesiology, 7(2):82-88.

Hull, M.W. and Reilly, M.G., 1968. Effect of repeated halothane anesthesia on sheep. American journal of veterinary research, 29(6):1161-1165.

Ivany, J.M. and Muir, W.W., 2004. Farm animal anesthesia. Farm Animal Surgery.Saunders, St. Louis, USA, pp.97-112.

Jones, H.D. and McLaren, C.A.B., 1965. Postoperative shivering and hypoxaemia after halothane, nitrous oxide and oxygen anaesthesia. BJA: British Journal of Anaesthesia, 37(1):35-41.

Kaiser-Klingler, S., 2007. Balanced anesthesia in small animals. Veterinary technician, 28(11):711-718.

Kästner, S.B.R., Von Rechenberg, B., Keller, K. and Bettschart-Wolfensberger, R., 2001. Comparison of medetomidine and dexmedetomidine as premedication in isoflurane anaesthesia for orthopaedic surgery in domestic sheep. Journal of Veterinary Medicine Series A, 48(4):231-241.

Kerr, C.L., Windeyer, C., Bouré, L.P., Mirakhur, K.K. and McDonell, W., 2007. Cardiopulmonary effects of administration of a combination solution of xylazine, guaifenesin, and ketamine or inhaled isoflurane in mechanically ventilated calves. American journal of veterinary research, 68(12):1287-1293.

Kharasch, E.D., 2008. Adverse drug reactions with halogenated anesthetics. Clinical Pharmacology and Therapeutics, 84(1):158-162.

Knill, R.L. and Clement, J.L., 1984. Site of selective action of halothane on the peripheral chemoreflex pathway in humans. Anesthesiology: The Journal of the American Society of Anesthesiologists, 61(2):121-126.

Knill, R.L. and Clement, J.L., 1985. Ventilatory responses to acute metabolic acidemia in humans awake, sedated, and anesthetized with halothane. Anesthesiology: The Journal of the American Society of Anesthesiologists, 62(6):745-753.

Kokkonen, U.M. and Eriksson, L., 1987. Cardiovascular and allied actions of xylazine and atropine in the unanaesthetized goat. Journal of veterinary pharmacology and therapeutics, 10(1):11-16.

Kutter, A.P., Kästner, S.B.R., Bettschart-Wolfensberger, R. and Huhtinen, M., 2006. Cardiopulmonary effects of dexmedetomidine in goats and sheep anaesthetised with sevoflurane. Veterinary record, 159(19):624-629.

Langley, M.S. and Heel, R.C., 1988, Propofol: A review of its pharmacodynamics and pharmacokinetic properties and use as an intravenous anaesthetic. Drugs 35: 334–372.

Larenza, M.P., Bergadano, A., Iff, I., Doherr, M.G. and Schatzmann, U., 2005. Comparison of the cardiopulmonary effects of anaesthesia maintained by continuous infusion of ketamine and propofol with anaesthesia maintained by inhalation of sevoflurane in goats undergoing magnetic resonance imaging, America Journal of Veterinary Research, 66(12):2135–2141.

Lemke, K.A., 2007, 'Anticholinergics and sedatives', in W.J. Tranquilli, J.C. Thurmon and K.A. Grimm (eds.), Lumb and Jones's veterinary anaesthesia and analgesia, 4th edition., Blackwell Publishing, Ames. pp. 203–239.

Lienhart, A., Fiez, N. and Deriaz, H., 1992, January. Frisson postopératoire: analyse des principaux facteurs associés. In Annales françaises d'anesthésie et de reanimation. Elsevier Masson. 11(5): 488-495.

Lin, H. C., Purohit, R. C., Powe, T. A., 1997. Anesthesia in sheep with propofol or with xylazine-ketamine followed by halothane. Veterinary surgery, 26(3): 247-252.

Lin, H. C., Pugh, D. G., 2002. Anesthetic management. In: Pugh DG, editor. Sheep and goat medicine. Philadelphia: WB Saunders. pp. 405–19.

Lin, H. and Walz, P., 2014. Farm animal anesthesia: cattle, small ruminants, camelids and pigs. John Wiley and Sons. p. 95.

Lin, H. C., Caldwell, F., Pugh, D. G., 2012. Anesthetic management. In Sheep and Goat medicine. 2nd edition. WB Saunders. pp, 517-538.

Lunam, C.A., Cousins, M.J. and Hall, P.D., 1985. Guinea-pig model of halothane-associated hepatotoxicity in the absence of enzyme induction and

hypoxia. Journal of Pharmacology and Experimental Therapeutics, 232(3):802-809.

Malik, V., 2010. Standardization of propofol and ketamine for constant rate infusion and their comparative evaluation with halothane anaesthesia in buffaloes. Indian Journal of Veterinary Surgery, 31(2):129.

Matsukawa, T., Kurz, A., Sessler, D.I., Bjorksten, A.R., Merrifield, B. and Cheng, C., 1995. Propofol linearly reduces the vasoconstriction and shivering thresholds. Anesthesiology: The Journal of the American Society of Anesthesiologists, 82(5):1169-1180.

Matthews, N.S., Gleed, R.D. and Short, C.E., 1986. Cardiopulmonary effects of general anesthesia in adult cattle. Modern veterinary practice, 67:618-620.

Matthews, N.S., Miller, S.M., Hartsfield, S.M. and Slater, M.R., 1992. Comparison of recoveries from halothane vsisoflurane anesthesia in horses. Journal of the American Veterinary Medical Association, 201(4):559-563.

Merin, R.G., Bernard, J.M., Doursout, M.F., Cohen, M. and Chelly, J.E., 1991. Comparison of the effects of isoflurane and desflurane on cardiovascular dynamics and regional blood flow in the chronically instrumented dog. Anesthesiology: The Journal of the American Society of Anesthesiologists, 74(3):568-574.

Mielck, F., Stephan, H., Buhre, W., Weyland, A. and Sonntag, H., 1998. Effects of 1 MAC desflurane on cerebral metabolism, blood flow and carbon dioxide reactivity in humans. British journal of anaesthesia, 81(2):155-160.

Mielck, F., Stephan, H., Weyland, A. and Sonntag, H., 1999. Effects of one minimum alveolar anesthetic concentration sevoflurane on cerebral metabolism, blood flow, and CO2 reactivity in cardiac patients. Anesthesia and Analgesia, 89(2):364-369.

Mohamadnia, A.R., Hughes, G. and Clarke, K.W., 2008. Maintenance of anaesthesia in sheep with isoflurane, desflurane or sevoflurane. Veterinary Record, 163(7):210-215.

Muir, W. W., 2007.Considerations for general anesthesia. In: Tranquilli, W. J., Thurman, J. C., Grimm, K. A., editors. Lumb and Jones' Veterinary Anesthesia and Analgesia. 4th edition. Ames, IA, USA: Blackwell. pp. 7–30.

Muir, W.W., Hubbell, J.A., Bednarski R. M., Lerche P. 2013. Handbook of Veterinary Anesthesia. Elsevier Health Sciences. p.163-187.

Murrell, J.C., Waters, D. and Johnson, C.B., 2008. Comparative effects of halothane, isoflurane, sevoflurane and desflurane on the electroencephalogram of the rat. Laboratory animals, 42(2):161-170.

Mutoh, T., Nishimura, R., Kim, H.Y., Matsunaga, S. and Sasaki, N., 1997. Cardiopulmonary effects of sevoflurane, compared with halothane, enflurane, and isoflurane, in dogs. American journal of veterinary research, 58(8):885-890.

Nakaigawa, Y., Akazawa, S., Shimizu, R., Ishii, R. and Yamato, R., 1995. Comparison of the effects of halothane, isoflurane, and sevoflurane on atrioventricular conduction times in pentobarbital-anesthetized dogs. Anesthesia and Analgesia, 81(2):249-253.

Natalini, C.C. and Pires, J.D.S., 2000. Comparative evaluation of the general anesthesia with halothane and isoflurane on the arterial pressure in dogs. Ciencia Rural (Brazil), 30(3):425-430.

Nolan, A.M., Reid, J. and Welsh, E., 1991. The use of propofol as an induction agent in goats. Journal of Veterinary Anaesthesia (United Kingdom). 18:53-54.

Offinger, J., Meyer, H., Fischer, J., Kästner, S.B., Piechotta, M. and Rehage, J., 2012. Comparison of isoflurane inhalation anaesthesia, injection anaesthesia and high volume caudal epidural anaesthesia for umbilical surgery in calves; metabolic, endocrine and cardiopulmonary effects. Veterinary anaesthesia and analgesia, 39(2):123-136.

Pablo, L.S., Bailey, J.E. and Ko, J.C., 1997. Median effective dose of propofol required for induction of anaesthesia in goats. Journal of the American Veterinary Medical Association, 211(1):.86-88.

Pablo, L.S., Ko, J.C.H. and Bailey, J.E., 1995. Determination of the induction dose ofpropofol in goats. In Proceedings of the Annual Meeting of the American College of Veterinary Anesthesiologists, Atlanta. p 29

Polis, I., Gasthuys, F., Laevens, H., Van Ham, L. and De Rick, A., 2001. The influence of ventilation mode (spontaneous ventilation, IPPV and PEEP) on cardiopulmonary

parameters in sevoflurane anaesthetized dogs. Journal of Veterinary Medicine Series A, 48(10):619-630.

Posner, L.P., 2007, 'Midazolam or diazepam – Which should I choose in my practice?', viewed 14 February 2008, from http://www.ivis.org/proceedings/navc/2007/SAE/031.asp?LA=1.

Posner, L.P., Moon, P.F., Bliss, S.P., Gleed, R.D. and Erb, H.N., 2003. Colloid osmotic pressure after hemorrhage and replenishment with Oxyglobin Solution, hetastarch, or whole blood in pregnant sheep. Veterinary anaesthesia and analgesia, 30(1):30-36.

Prassinos, N.N., Galatos, A.D. and Raptopoulos, D., 2005. A comparison of propofol, thiopental or ketamine as induction agents in goats, Veterinary Anaesthesia and Analgesia 32:289–296.

Ramachandra, V., Moore, C., Kaur, N. and Carli, F., 1989. Effect of halothane, enflurane and isoflurane on body temperature during and after surgery. British journal of anaesthesia, 62(4):409-414.

Reid, J., Nolan, A.M. and Welsh, E., 1993. Propofol as an induction agent in the goat: a pharmacokinetic study. Journal of Veterinary Pharmacology and Therapeutics, 16(4):488-493.

Rezakhani, A., Edjtehadi, M. and Szabuniewicz, M., 1977. Prevention of thiopental and thiopental/halothane cardiac sensitization to epinephrine in the sheep. Canadian Journal of Comparative Medicine, 41(4):.389.

Riazuddin, M.D., William, B.J. and Ameerjan, K., 2004. Studies on halothane-isoflurane anaesthesia in dorsal and lateral recumbency in cattle. Indian Journal of Veterinary Surgery, 25(2):75-76.

Riebold, T. W. 2007. Ruminants. In: Tranquilli, W. J., Thurmon, J. C., Grimm, K. A., editors. Lumband Jones' veterinary anesthesia and analgesia. 4th edition. Ames (IA): Blackwell; pp. 731–746.

Riebold, T. W., 2015. Anesthesia and analgesia for domestic species: ruminants. In: Grimm K. A., Lamont L. A., Tranquilli W. J., Greene S. A., Robertson S. A., editors. Lumb and Jones' Veterinary anesthesia and Analgesia. 5th edition. Ames, IA, USA: Blackwell; pp. 912–927.

Roald, O.K.,Forsman, M., Heier, M.S. and Steen, P.A., 1991. Cerebral effects of nitrous oxide when added to low and high concentrations of isoflurane in the dog. Anesthesia and Analgesia, 72(1):75-79.

Robinson, S.L., Richardson, C.A., Willis, M.M. and Gregory, G.A., 1985. Halothane anesthesia reduces pulmonary function in the newborn lamb. Anesthesiology: The Journal of the American Society of Anesthesiologists, 62(5):578-581.

Rugh, K. S., Zinn, G.M., Paterson, J. A and Thome, J.G., 1985. Inhalant anaesthetics in cattle. Laboratory Animal Science. 35:178–181.

Schieber, R.A., Namnoum, A., Sugden, A., Shiu, G.K., Orr, R.A. and Cook, D.R., 1986. Hemodynamic effects of isoflurane in the newborn piglet: comparison with halothane. Anesthesia and analgesia, 65(6):633-638.

Short, C. E., 1986. Preanesthetic medications in ruminants and swine. The veterinary clinics of North America. Food animal practice, 2:553-566.

Singh, G.D., Kinjavdekar, P., Aithal, H.P., Pawde, A.M., Zama, M., Singh, J. and Tiwary, R., 2013. Clinicophysiological and haemodynamic effects of fentanyl with xylazine, medetomidine and dexmedetomidine in isoflurane-anaesthetised water buffaloes (Bubalusbubalis). Journal of the South African Veterinary Association, 84(1):1-11.

Smith, M.C. and Sherman, D.M., 1994. Blood, lymph and immune systems. Goat Medicine. 1st edition. Philadelphia, Lea andFebiger, pp.193-229.

Steffey, E. P, Howland, D., 1979. Halothane anaesthesia in calves. American Journal of Veterinary Research. 40(3):372–376.

Steffey, E. P., Mama, R. M. 2007. Inhalation anesthetics. In: Tranquilli, W. J., Thurmon, J. T., Grimm, K. A. editors. Lumb and Jones' Veterinary Anesthesia and Analgesia, 4th edition. Ames: Blackwell; pp. 355–394.

Steffey, E.P. and Howland Jr, D., 1978. Potency of enflurane in dogs: comparison with halothane and isoflurane. American journal of veterinary research, 39(4), p.573-577.

Steffey, E.P. and Howland Jr, D., 1979. Halothane anesthesia in calves. American Journal of Veterinary Research, 40(3):372-376.

Steffey, E.P., 2002. Recent advances in inhalation anesthesia. The Veterinary Clinics of North America. Equine Practice, 18(1):.159-168.

Steffey, E.P., Hodgson, D.S., Dunlop, C.I., Miller, M.F., Woliner, M.J., Heath, R.B. and Grandy, J., 1987.Cardiopulmonary function during 5 hours of constant-dose isoflurane in laterally recumbent, spontaneously breathing horses. Journal of veterinary pharmacology and therapeutics, 10(4):290-297.

Steffey, E.P., Kelly, A.B. and Woliner, M.J., 1987. Time-related responses of spontaneously breathing, laterally recumbent horses to prolonged anesthesia with halothane. American Journal of Veterinary Research, 48(6):952-957.

Stegmann, G.F., 2004. Midazolam/ketamine induction and isoflurane maintenance of anaesthesia in a 2-month-old, hand-raised African buffalo (Synceruscaffer): clinical communication. Journal of the South African Veterinary Association, 75(1):43-44.

Stevens, W.C., 1972. New halogenated anesthetics: enflurane and isoflurane. California Medicine, 117(4):47.

Stoelting, R. K., 1991. Inhaled anaesthetics. In: Stoelting R. K., editor. Pharmacology and physiology in anaesthetic practice. 2nd ed. Philadelphia, PA: Lippincott; p. 33–69.

Takase, K., 1976. Studies on halothane inhalation anesthesia in cattle. Bulletin of Azabu Veterinary College.31:1-34.

Taylor, P.M., 1991. Anaesthesia in sheep and goats. In Practice, 13(1):.31-36.

Thurmon, J.C. and Benson, G., 1993. Anesthesia in ruminants and swine. In: Howard, J. L., editor. Current veterinary therapy, 3:food animal practice, Philadelphia: WB Saunders; pp.58-76.

Thurmon, J.C. and Benson, G.J., 1986. Anesthesia in ruminants and swine. In: Howard, J. L., editor. Current Veterinary Therapy, 2: food animal practice, Philadelphia: WB Saunders; pp.51-57.

Tranquilli, W.J., 1986. Techniques of inhalation anesthesia in ruminants and swine. Veterinary Clinics of North America: Food Animal Practice, 2(3):593-619.

Tranquilli, W. J., Thurmon, J. C., and Benson, C. J. 1985. Alterations in the arrythmogenic dose of epinephrine induced by xylazine and specific adrenergic

receptor antagonists in halothane-anesthetized pigs. In: Proceedings of the Second International Congress of Veterinary Anesthesiologists. Pp. 92

Trim, C.M., 1981. Sedation and general anesthesia in ruminants. The bovine practitioner, 16:137-144.

Trim, C.M., 1987. Special anesthesia considerations in the ruminant. In Short, C. E. editors. Principles and practice of veterinary anesthesia, Baltimore, Williams and Wilkins; pp.285-300.

Valverde, A. and Doherty, T.J., 2008. Anesthesia and analgesia of ruminants. In Fish, R., Danneman, P. J., Brown, M., editors.Anesthesia and analgesia in laboratory animals. 2nd edition. London: Academic Press; pp. 385-411.

Vesal, N., Spadavecchia, C., Steiner, A., Kirscher, F. and Levionnois, O.L., 2011. Evaluation of the isoflurane-sparing effects of lidocaine infusion during umbilical surgery in calves. Veterinary anaesthesia and analgesia, 38(5):451-460.

Wade, J.G. and Stevens, W.C., 1981.Isoflurane: an anesthetic for the eighties? Anesthesia and analgesia, 60(9):666-682.

Wagner, A.E., Dunlop, C.I., Wertz, E.M., Chapman, P.L., Baxter, G.M. and Klopp, L.S., 1995. Hemodynamic responses of horses to anesthesia and surgery, before and after administration of a low dose of endotoxin. Veterinary Surgery, 24(1):78-85.

Wagner, A.E., Muir 3rd, W.W. and Hinchcliff, K.W., 1991. Cardiovascular effects of xylazine and detomidine in horses. American journal of veterinary research, 52(5):651-657.

Waterman, A.E., 1988. Use of propofol in sheep. Veterinary Record, 122(11):260-260.

West, G., Heard, D.J. and Caulkett, N. 2014. Zoo animal and wildlife immobilization and anesthesia. John Wiley and Sons. p. 7-10.

White, P.F., 2008. Propofol Its Role in Changing the Practice of Anesthesia. Anesthesiology: The Journal of the American Society of Anesthesiologists, 109(6):1132-1136.

Whitehair, K.J., Steffey, E.P., Willits, N.H. and Woliner, M.J., 1993. Recovery of horses from inhalation anesthesia. American journal of veterinary research, 54(10):1693-1702.

WHO, 2010. World Health Organisation's list of core medicines (WHO, 2010). Available from: http://www.who.int/ medicines/publications/ essentialmedicines/en/index.html.

Wolff, W.A., Lumb, W.V. and Ramsay, M.K., 1968. Comparison of halothane and chloroform anesthesia in horses. American journal of veterinary research, 29(1):125-132.

Young, W.L., 1992. Effects of desflurane on the central nervous system. Anesthesia and analgesia, 75(4):32-S37.

Annex-I

A questionnaire for the surgery with gaseous anesthesia in small ruminants

Case No. Case Reg. No. Date:

Owner name: Address: Mobile No:

Species: Breed: Age:

Sex: Body weight: BCS:

Anamnesis/Clinical History:

Onset: Sudden/Gradual Duration of illness:

Defecation: Y/N Urination: Y/N

F/H: Normal/Loss of Appetite/Off-fed/Other…….

Roughage (Y/N)……kg/day Concentrate (Y/N)……kg/day

Housing System: Intensive/Semi-intensive/Tethered/Cyanotic/Other……

History of apnea: Y/N Exercise tolerance: Y/N

Clinical Examination:

Heart rate:……..beats/min Respiratory rate: ……..breaths/min

Pulse rate: ……. Rectal temperature: ……˚F

Visible mucus membrane: Pale/Pink/Icteric/Cyanotic/Other…..

General attitude: Alert/Dull/Depressed/Other……..

Dehydration: Normal/Mild/Moderate/Severe

Posture: Normal/Defective Gait: Normal/Lameness

Additional Findings:

Diagnosis:

Annex II

Chattogram Veterinary and Animal Sciences University

Sahidul Alam Quaderi Teaching Veterinary Hospital, Khulshi-4225, Chittagong

Anesthesia Record Sheet

Name of Surgery/Operation:

Patient description:

Surgeon:

Date of registration: ID No:

Species: Breed: Age:

Assistant:

Sex: Weight:

Anesthesiologist:

Pre-anesthetic evaluation of patient:

Tem: Pulse rate: Respiration rate: MM color: CRT (sec):

Other findings:

	Time	Dose (mg/kg)	Calc. volume (ml)	Route	Effect/Remarks
Premedication					Sedation: Mild/Moderate/Profound Vomiting: Y/N
Induction					
Maintenance					

Time (Hrs.) (min)	0	15	30	45	1	15	30	45	2	15	30
Anesthetics % (Iso/Hal)											
Oxygen flow rate (L/min)											
$SpO_{2\%}$											
$EtCO_{2\ mmHg}$											
Temperature (^0F)											

Cardiovascular parameters

O Pulse/heart rate

V Systolic pressure

= Mean pressure

∧ Diastolic pressure

200 180 160 140 120 100 95 85 75 65

Respiratory rate × (Breath/min)

Intubated: Y / N

ET tube size: **Complications** Bradycardia ( ) Tachycardia ( ) Hypotension ( ) Apnea ( ) Hypoventilation ( ) Hypoxia ( )	55 45 35 25 15 5																													
Anesthesia Depth Light/Medium/Deep																														
CRT (sec)																														
Fluid (ml given in 15min/Running total)																														

Recovery:

Time from anesthetic cessation to Swallowing reflex……...min,

Sternal recumbency……..min,

Standing .....……..min.

Immediate PO condition:

Quiet and calm / excitement / struggle / others……

Complications during recovery:

None / respiratory obstruction / Delayed recovery

Others…….

Total Fluid volume.....

Surgical time (skin to skin): ……...hr..... min

Anesthesia time (induction to return of swallowing reflex): ……hr……min.

Annex III

Values of heart rate (HR) in small ruminants during halothane and isoflurane maintenance anesthesia.

HR by 5-min intervals, (Beats/min)	**Group 1 (Halo) Mean±SD**	**Group 2 (ISO) Mean±SD**
HR 0	92.2±5.26[a]	112.8±14.06[b]
HR 5	92±5.15[a]	118.6±12.18[b]
HR 10	91.4±6.43[a]	114.4±11.37[b]
HR 15	91.6±5.32[a]	112.4±7.02[b]
HR 20	90.6±6.43[a]	114±7.38[b]
HR 25	90.4±5.22[a]	119.2±14.81[b]
HR 30	90.4±5.55*[a]	117.2±17.25[b]
HR 35	90.2±4.87*[a]	118±16.23[b]
HR 40	90±4.36[a]	117.4±15.58[b]
HR 45	89.6±4.39*[a]	119.8±17.81[b]
HR 50	89±4.42*[a]	119.6±17.14[b]
HR 55	88.2±5.07**[a]	119.6±15.71[b]
HR 60	88±4.47**[a]	117.8±12.62[b]

*: Differs significantly ($p<0.05$) from base value.
**: Differs significantly ($p<0.01$) from base value.
[a, b:] Differs significantly ($p< 0.05$) between the two groups at corresponding intervals.

Annex IV

Values of respiratory rate (RR) in small ruminants during halothane and isoflurane maintenance anesthesia.

RR by 5-min intervals, (Breath/min)	**Group 1 (Halo) Mean±SD**	**Group 2 (ISO) Mean±SD**
RR 0	18.4±6.35	19.8±2.17
RR 5	17±4.34	21.4±5.03
RR 10	16.4±4.39	20±3.39
RR 15	15.4±5.37	18.4±4.04
RR 20	17.2±5.97	18±4.36
RR 25	17.6±5.59	18.6±3.29
RR 30	18.4±4.10	19.8±3.56
RR 35	17.2±5.12	18.4±3.05
RR 40	15±4.00	17±5.24
RR 45	14.6±4.39	15.2±3.96
RR 50	15.6±2.30	17.6±5.18
RR 55	14±3.39	17.8±3.63
RR 60	14.2±4.15*	17.2±3.90

*: Differs significantly ($p<0.05$) from base value.
**: Differs significantly ($p<0.01$) from base value.
[a, b:] Differs significantly ($p< 0.05$) between the two groups at corresponding intervals.

Annex V

Values of Oxygen saturation (SpO2) in small ruminants during halothane and isoflurane maintenance anesthesia.

SpO2 by 5-min intervals, %	**Group 1 (Halo)** **Mean±SD**	**Group 2 (ISO)** **Mean±SD**
SpO2 0	98.6±0.55	98.4±0.55
SpO2 5	97.6±2.30	97.2±1.30
SpO2 10	97.2±1.79	97.4±1.52
SpO2 15	96.8±1.64	98.2±1.64
SpO2 20	98±1.22	98.2±1.48
SpO2 25	98±1.22	98.6±0.89
SpO2 30	98±1.00	98.8±1.30
SpO2 35	98.2±0.84	98.2±1.48
SpO2 40	97.8±1.10	97.4±1.52
SpO2 45	97.6±1.14	98±1.87
SpO2 50	97.8±0.45	98±1.41
SpO2 55	98.4±0.89	98.4±0.55
SpO2 60	98±0.71	98.8±0.84

*: Differs significantly ($p<0.05$) from base value.
**: Differs significantly ($p<0.01$) from base value.
[a, b:] Differs significantly ($p< 0.05$) between the two groups at corresponding intervals.

Annex VI

Values of Systolic arterial pressure (SAP) in small ruminants during halothane and isoflurane maintenance anesthesia.

SAP by 5-min intervals, %	**Group 1 (Halo)** **Mean±SD**	**Group 2 (ISO)** **Mean±SD**
SAP 0	81.4±14.33	102±15.48
SAP 5	77.6±8.76[a]	107.2±8.11[b]
SAP 10	70.8±7.79[*a]	109.6±7.64[b]
SAP 15	62.2±13.62[*a]	106.2±15.53[b]
SAP 20	64±10.05[*a]	107.6±11.13[b]
SAP 25	65±9.92[*a]	110.6±11.97[b]
SAP 30	68.4±10.19[a]	110±12.59[b]
SAP 35	71.6±9.61[a]	111.4±8.29[b]
SAP 40	72.8±10.13[a]	110±13.80[b]
SAP 45	79.8±23.30	109±22.48
SAP 50	76.8±18.83[a]	114.2±9.09[b]
SAP 55	78.4±12.38[a]	117.6±7.33[b]
SAP 60	79.6±7.50[a]	116.2±11.67[b]

*: Differs significantly ($p<0.05$) from base value.
**: Differs significantly ($p<0.01$) from base value.
[a, b:] Differs significantly ($p< 0.05$) between the two groups at corresponding intervals.

Annex VII

Values of Diastolic arterial pressure (DAP) in small ruminants during halothane and isoflurane maintenance anesthesia.

DAP by 5-min intervals, %	**Group 1 (Halo) Mean±SD**	**Group 2 (ISO) Mean±SD**
DAP 0	49.6±11.99	63.8±9.20
DAP 5	48±7.94[a]	67.8±7.09[b]
DAP 10	40.4±11.17[a]	70.6±5.98[b]
DAP 15	38±13.51[a]	71.8±15.58[b]
DAP 20	34.2±11.12[a]	72.6±9.32[b]
DAP 25	33.4±8.17[*a]	78.6±15.96[b]
DAP 30	35.8±11.37[a]	76.8±15.85[b]
DAP 35	37±10.07[a]	79.8±21.46[b]
DAP 40	41.8±14.24[a]	75.8±17.57[b]
DAP 45	47.6±20.91[a]	78.6±22.35[b]
DAP 50	40.6±8.38[a]	79.6±15.24[b]
DAP 55	42.6±4.15[a]	83.8±11.10[b]
DAP 60	44.6±6.66[a]	82.8±14.94[b]

*: Differs significantly ($p<0.05$) from base value.
**: Differs significantly ($p<0.01$) from base value.
[a, b:] Differs significantly ($p< 0.05$) between the two groups at corresponding intervals.

Annex VIII

Values of Mean arterial pressure (MAP) in small ruminants during halothane and isoflurane maintenance anesthesia.

MAP by 5-min intervals, %	**Group 1 (Halo)** **Mean±SD**	**Group 2 (ISO)** **Mean±SD**
MAP 0	62.2±14.17	81.6±11.89
MAP 5	58.4±8.38[a]	85.2±4.60[b]
MAP 10	52.4±10.31[a]	86.8±5.22[b]
MAP 15	49.2±10.73[a]	82.8±14.86[b]
MAP 20	45.6±9.99[a]	86±6.82[b]
MAP 25	44.8±8.01[*a]	90.6±15.42[b]
MAP 30	48.6±10.41[a]	90±14.95[b]
MAP 35	49±9.62[*a]	94.2±10.89[b]
MAP 40	51.6±11.10[a]	89.4±14.26[b]
MAP 45	60.4±23.46	89.4±22.55
MAP 50	51.4±7.99[a]	91.4±14.36[b]
MAP 55	50.75±6.02	98.6±8.44
MAP 60	52.6±2.88	97.6±11.52

*: Differs significantly ($p<0.05$) from base value.
**: Differs significantly ($p<0.01$) from base value.
[a, b:] Differs significantly ($p< 0.05$) between the two groups at corresponding intervals.

Annex IX

Values of Temperature in small ruminants during halothane and isoflurane maintenance anesthesia.

Temperature by 5-min intervals, (˚C)	**Group 1 (Halo) Mean±SD**	**Group 2 (ISO) Mean±SD**
Temperature 0	100.34±1.17	100.96±0.92
Temperature 5	100.56±0.77	100.88±0.64
Temperature 10	99.8±1.73	100.52±0.69
Temperature 15	99.04±2.34	100.04±0.62*
Temperature 20	99.22±1.23**	99.6±0.58**
Temperature 25	99.04±1.23**	99.12±0.43**
Temperature 30	98.74±1.11**	99.04±0.79**
Temperature 35	98.3±1.21**	99.06±0.78*
Temperature 40	98.5±0.98**	98.82±0.42*
Temperature 45	97.84±1.25**a	98.76±0.36**b
Temperature 50	97.76±0.56**a	98.64±0.35**b
Temperature 55	97.88±0.55**	98.82±0.61**
Temperature 60	98.02±0.41*	98.48±0.50**

*: Differs significantly ($p<0.05$) from base value.
**: Differs significantly ($p<0.01$) from base value.
a, b: Differs significantly ($p< 0.05$) between the two groups at corresponding

Annex X

Recovery data comparing halothane (HAL) vs. isoflurane (ISO) in small ruminants.

Parameter	Time in minute HAL (n=10)	Time in minute ISO(n=10)
Extubation	8.9±0.74	6.2±1.30*
First head movement	13.4±2.51	12.6±1.82
Thoracic recumbency	20.2±2.28	17.2±1.30*
Standing up	27.2±1.92	22.8±3.27*

Data are expressed as mean±SD.
*: Significant difference between the anesthesia agents ($P < 0.05$).

Biography

DR. Joya Chowdhury is the daughter of Himangshu Bimal Chowdhury and Rekha Rani Dutta. She is an MS Student of Surgery under the Department of Medicine and Surgery at Chattogram Veterinary and Animal Sciences University (CVASU). She had successfully completed her DVM degree in 2017 from CVASU. At present she is working as a lecturer of Surgery under the faculty of Veterinary and Animal Sciences in Gono Bishwabidyalay. Her research and publications are based on the veterinary surgery and anesthesiology. She has a great interest on veterinary anesthesiology.