Comparison of Anesthetic Potency and Cardiopulmonary Effects of Halothane and Isoflurane Anesthesia in Dogs

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Session: 2018-2019

A thesis submitted for the partial fulfillment of the requirements for the degree of Master of Science (MS) in Surgery

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June 2020

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DR. Aparna Datta

June, 2020

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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 & My

Beloved Parents

Acknowledgements

First and foremost , all praises and thanks to the Almighty “God ’’ for His blessings throughout the research work to complete the research successfully for the degree of Master of Science (MS) in Surgery under the Department of Medicine and Surgery, Chattogram Veterinary and Animal Sciences University (CVASU) .

I would like to express my heartfelt gratitude, profound appreciation and indebtedness to my research supervisor **Dr. Bibek Chandra Sutradhar,** Professor, Department of Medicine and Surgery, CVASU for his meticulous guidance, incessant support, encouragement and expert planning right from selection of my work to the successful completion of the manuscript. I am grateful for his perseverance and consideration shown to me.

I am greatly obliged to **Dr. Tuli Dey**, Assistant professor, Department of Medicine and Surgery as a co-supervisor of my study, for her valuable advice and cooperation during my study. Special thanks to **Prof. Dr. Bhajan Chandra Das**, Director, Teaching Veterinary Hospital, CVASU.

I would like to acknowledge my special thanks to Dr. Sushyam Biswas, Dr. Joya Chowdhury, Dr. Sreekanta Biswas, Dr. Sabiha Zarin Tasnim, Dr. Shouvo Singha, Dr. Bayazid Bostami, for their constant help and support during the research work.

I sincerely thankful to the Coordinator of Advance Studies and Research for providing research fund to complete my research work.

I am also thankful to the staff of the Department of Medicine and Surgery and Teaching and Training Pet Hospital and Research Center, CVASU for their help during my work.

I am forever indebted to my parents and brother for their unfailing love, support and encouragement. I pay my respect to all those researchers in whose writings I had gained knowledge.

The Author

June, 2020

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LIST OF ABBREVIATIONS AND SYMBOLS

CVASU	**Chittagong Veterinary and Animal Sciences University**
SAQTVH	**Shahidul Alam Quadery Teaching Veterinary Hospital**
TTPHRC	**Teaching and Training Pet Hospital and Research Center**
BW	**Body weight**
mm	**Millimetre**
kg	**Kilogram**
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**
%	**percent**
˚C	**Degree Celsius**
˚F	**Degree Fahrenheit**
***et al*.**	**And his associates**
HAL	**Halothane**
ISO	**Isoflurane**

Abstract

The study was conducted at SAQ Teaching Veterinary Hospital (SAQTVH), Chattogram and Teaching & Training Pet Hospital and Research Center (TTPHRC) Dhaka, CVASU, to evaluate anesthetic potency and cardiopulmonary effects of isoflurane and halothane anesthesia in dogs. Fourteen dogs were randomly selected that were admitted to these two hospitals. They were allocated into two anesthesia groups (n = 7 in each group). Dogs were premeditated with xylazine hydrochloride (1 mg/kg) intramuscularly and anesthesia was induced by propofol (2 mg/kg, IV). Inhalation anesthesia was maintained for a routine surgical procedure using 2% isoflurane (ISO) and 2.5% halothane (HAL). Cardiopulmonary parameters [heart rate (HR), respiratory rate (RR), systolic arterial pressure (SAP), diastolic arterial pressure (DAP), mean arterial blood pressure (MAP), oxygen saturation (SpO_2), body temperature] were monitored and recorded during routine surgery for every 5 minutes interval up to completion of surgery. No significant difference was found between HAL and ISO groups in SPO_2 ($p>0.1$). Pulmonary indices during isoflurane anesthesia caused a significant increase (44.7±7.8 breath/min) in the respiratory rate in comparison to halothane anesthesia. There was no significant difference in HR between the two anesthetic groups. Systolic arterial pressure (SAP), diastolic arterial pressure (DAP), mean arterial blood pressure (MAP) were almost the same in both groups. Body temperature decreased gradually during ISO and HAL anesthesia without significant difference. Therefore, it is concluded that, halothane and isoflurane, both can be safe anesthetics for dogs with minimum side effects on cardiovascular and respiratory systems during routine surgical treatment in veterinary hospital. The result from this research may help the practitioners to increase awareness of anesthetic management in practices.

Keywords: Cardiopulmonary effects, Halothane, Isoflurane, Dogs

Chapter I

Introduction

Very impressive progress has been developed in diagnostic as well as surgical techniques in the last decades (Polis et al., 1999). As a consequence, the necessity of a safe and stable long-standing anesthesia is needed for diagnostic as well as surgical techniques. The majority of companion animals will undergo general anesthesia at least once in their lifetime (Polis et al., 1999). In addition to routine procedures and surgery, general anesthesia is increasingly required in canine patients to facilitate advanced diagnostic and therapeutic interventions (Bille et al., 2012). Inhalation anesthetics are very useful for this purpose. Inhalation anesthetics are considered over injectable agents because of their rapid induction, rapid recovery with better control over the depth and duration of anesthesia and also more desirable physiologic responses (Breck et al., 2003). Despite the progressive need for general anesthesia, over the last two decades, in total canine anesthetic mortality rates have not declined (Dyson et al., 1998, Brodbelt et al., 2008, Bille et al., 2012).

A standard premedication with the anesthetic protocol included pre-anaesthetics drugs have major importance under clinical circumstances. A premedication drug reduces stress before induction of anesthesia, facilitates manipulations and also contributes to a smooth induction and recovery from anesthesia. Either inhalant or injectable anesthetics are used alone or in combination for induction of anesthesia in dogs. Induction technique could allow rapid endotracheal intubation with minimal cardiopulmonary depression or other undesirable side effects. Inhalation anesthetics are used extensively for the anesthetic management of animals because of their rapid induction, rapid recovery with better control over the depth and duration of anesthesia (Stewart and James 2003). Among the anesthetic drugs, inhalation anesthetics are unique because after anesthesia a large part of the anesthetic is removed from the body, via lungs (Steffey and Mama 2007).

The pharmacokinetic characteristics of inhalation anesthetics are predictable and rapid adjustment of anesthetic depth (Steffey and Mama 2007). The inhaled agents are supplied to the patients through a special apparatus. A source of oxygen (O2) and a patient breathing circuit with a endotracheal tube or face mask are attached with this apparatus with proper elimination of carbon dioxide (CO2). All of these apparatus

help to minimize patient morbidity or mortality because they improved arterial oxygenation and facilitate lung ventilation (Steffey and Mama 2007). Inhalation anesthesia induces a dose-related cardiopulmonary depression in all animals (Polish et al., 2001). Halogenated anesthetics, like halothane and isoflurane, can change the cardiac rate and rhythm (Nakaigawa et al., 1995). In veterinary medicine, halothane (HAL) and isoflurane (ISO) are commonly used in clinical practice (Mutoh et al., 1997).

Halothane has been used for several decades and is still a valuable anesthetic in many clinical practices. After its development for human anaesthesia by Sweking in 1951, halotane was first used in veterinary anaesthesia, in 1956 (Suckling, 1957). Halothane is a non-explosive and relatively stable anesthetic and low blood-gas solubility. It provides smooth and rapid induction and recovery from anaesthesia and the incidence of postoperative nausea and vomiting is low and relatively less toxic than previously used inhalant anaesthetic agents like (eg. Methoxyflurane, diethyl ether, chloroform). Halothane can be used in a closed-circuit system and does not react with soda lime. It causes a dose-dependent cardiopulmonary depression (Short, 1987). Halothane having the lowest respiratory depression effect and low airway irritation among inhalation anaesthetics while isoflurane and desflurane induce airway-irritation (Harper, 2004).

Halothane induces dose-dependent depression of CNS. It Increases cerebral blood flow with bradycardia at clinical concentration. Hypotension is depended on the depth of anesthesia and decreased myocardial contractility at low concentration and also causes vasodilatation at high concentration (Muir et al., 2013). Halothane sensitizes the heart to catecholamine-induced arrhythmias. It has teratogenic effects and crosses the placental barrier. These anesthetics have potential risks in canine and feline pregnancy (Papich, 1992). Halothane is contraindicated in patients with malignant hyperthermia or significant hepatotoxicity (Plumb and Pharm, 2011). Complications have been reported in halothane anesthesia, especially halothane causes hepatitis (Voigt et al., 1997, Otedo, 2004, Kumar et al., 2005). In developing countries, halothane is even considered for use, due to it is a least expensive inhalation anaesthetic and minimum alveolar concentration (MAC) is less (0.89) compare to the other inhalation anaesthetics (Harper, 2004).

In veterinary medicine, isoflurane is generally preferred as the most widely used inhalation anesthetic (Steffey and Mama, 2007). To anesthetize domestic animals and humans isoflurane is commonly used and sometimes it is used for immobilizing smaller wild animals (Belant, 1995; Gaynor et al., 1997; Kreeger et al., 1998). Isoflurane was promoted by Terrell, in the early seventies (Wade and Stevens, 1981). It is 1-chloro-2-trifluoroethyl-difluoromethyl ether, is an isomer of enflurane (Hellebrekers, 1986). It is a less reactive, more potent and non-inflammable volatile anaesthetic agents. Due to relatively low blood-gas solubility of the isoflurane, it consent for rapid and smooth induction and recovery and enables quick change in depth of anesthesia (Seal and Kreeger, 1987) and does not sensitize the heart to catecholamine-induced arrhythmias (Eger, 1981; Wade and Stevens, 1981) less organ toxic (Mazzer et al., 1974).

It has been reported, isoflurane has cardiovascular and respiratory side-effects from the use (Klide, 1976; Steffey and Howland, 1977; Stevens et al., 1971). Isoflurane has been demonstrated to have less myocardial depressant properties (Merin et al., 1991). It is rapidly absorbed and distributed into the CNS and crosses the placenta and is primarily eliminated unchanged via the lungs alveoli; only about 0.17% is metabolized in the liver and very little biodegradation and formed inorganic fluoride (trifluoroacetic acid). Isoflurane induces excellent muscle relaxation. In the gastrointestinal system, it decreased smooth muscle tone and motility; no hepatotoxicity and minimal postanesthetic changes in renal function are reported due to minimal metabolism, however, renal blood flow is dose-dependently (Muir et al., 2013).

Some animal studies have reported that isoflurane may be fetotoxic (Papich, 1992), although it seems to be safe in dogs and cat in early pregnancy (Papich, 1992) Isoflurane is contraindicated in patients with a history of malignant hyperthermia increased CSF or head injury, or myasthenia gravis. It can be irritating to the respiratory system and not recommended for mask induction (Clarke, 2008). Isoflurane causes hypotension; secondary to vasodilation is considered to be dose-dependent. Dose-related respiratory depression, and GI effects like nausea, vomiting have been reported in Isoflurane ansthesia of the dog (Plumb and Pharm, 2011).

To facilitate clinical anesthesia, dogs used in this study were premedicated with xylazine HCl and then induction with propofol. Xylazine HCl can cause changes in heart rate and blood pressure (Klide et al., 1975) and Propofol may cause hypotension, bradycardia followed by reflex tachycardia, dose-dependent decreases in arterial blood pressure and arrhythmias in the cardiovascular system (Muir et al., 2013). In this study, dogs were anesthetized with xylazine HCl and propofol and maintained with isoflurane or halothane. We compared the cardiovascular and respiratory effects of halothane and isoflurane anesthesia in dogs during different surgical procedures in our veterinary hospitals. Therefore, the use of isoflurane and halothane as inhalation anesthetics can be potential use for the dog and also helpful to reduce anesthetics risk during surgery as well as in postoperative management.

Therefore, the research was conducted to evaluate and compare the anesthetic effects of halothane and isoflurane anesthesia on certain cardiopulmonary parameters along with anesthetic potency in dogs.

Chapter II

Review of Literature

The word anesthesia, comes from the Greek word *anaisthaesia*, meaning "insensibility," means the loss of sensation to the whole or any part of the body. Anesthesia which is induced by drugs that depress the action of nervous tissue locally, regionally, or within the central nervous system (CNS). General anesthesia is a reversible drug-induced unconsciousness which is characterized by depression of the CNS and analgesia. In this situation, the patient is not arousable by noxious stimulation (John and Charles, 2007).

The aim of administering an inhalation anaesthetic agent to a patient is to achieve an adequate partial pressure of anaesthetic in the brain to cause a desired level of central nervous system depression. Until establishment of the equilibrium above the several compartments, inhalation anesthetics are move down a sequence of partial pressure gradients from state of higher tension to those of lower tension. The anaesthetic agent moves from the vaporizer to breathing circuit, from breathing circuit to lungs, from lungs to arterial blood, and lastly, from arterial blood to body tissues.

2.1 Inhalant anesthetics

Inhalation anesthetic means gases or vapors are inhaled in combination with oxygen. Inhalantion anesthetics are generally used in companion animal veterinary practice. They are considered over injectable agents because of their rapid induction, rapid recovery with better control over the depth and duration of anesthesia and also more desirable physiologic responses (Sedgwick, 1986). Despite the increasing need for general anesthesia, overall canine anesthetic mortality rates have not declined over the last two decades (Dyson et al., 1998; Brodbelt et al., 2008; Bille et al., 2012). A standard premedication with the anesthetic protocol included pre-anaesthetics drugs have major importance under clinical circumstances.

A premedication drug reduces stress before induction of anesthesia, facilitates manipulations and also contributes to a smooth induction and recovery from anesthesia. Either inhalant or injectable anesthetics are used alone or in combination for induction of anesthesia in the dogs. Induction technique could allow rapid

endotracheal intubation with minimal cardiopulmonary depression or other undesirable side effects (Steffey and Mama, 2007). Inhalation anesthetics are used extensively for the anesthetic management of animals. Among the anesthetic drugs, inhalation anesthetics are unique because they are administered, and in large part removed from the body, via the lungs (Steffey and Mama, 2007).

The inhaled agents are supplied to the patients through a special apparatus. A source of oxygen (O2) and a patient breathing circuit with an endotracheal tube or face mask are attached with this apparatus with proper elimination of carbon dioxide (CO2). All of these apparatus help to minimize patient morbidity or mortality because they improved arterial oxygenation and facilitate lung ventilation (Steffey and Mama, 2007). Inhalation anesthesia induces a dose-related cardiopulmonary depression in all animals (Polish et al., 2001). Halogenated anesthetics, like halothane and isoflurane, can change the cardiac rate and rhythm (Nakaigawa et al., 1995). In veterinary medicine, halothane (HAL) and isoflurane (ISO) have been used in clinical practice (Mutoh et al., 1997).

2.2 Mechanism of Action of Inhalation Anesthetics

The specific mode of action of most anesthetics is remains unknown. Some experimental work has engaged a protein “target” on a verities population of ionophores that is essential for anesthetic action (Franks and Lieb, 2004). Protein receptors in the central nervous system are responsible for the mechanism of action of inhaled anesthetics (West et al., 2014). This pinciple is adopted by the steep dose–response curve for inhaled anesthetics. Here inhaled agents disrupt ion flow by an indirect action, via a second messenger on the lipid membrane through membrane channels, or by direct and specific binding to channel proteins.

Another theory, volatile agents may activate or facilitate gamma-aminobutyric acid (GABA) channels, resulting in hyperpolarized cell membranes. They may inhibit certain calcium channels, preventing the release of neurotransmitters and inhibit glutamate channels (West et al., 2014). Consequent of Franks and Lieb investigation, a wide range of inhalant anesthetics suppressed the water-soluble enzyme firefly luciferase (Franks and Lieb, 1984). This enzyme hydrolyzes luciferin to create light

and is often a model for anesthetic action because the rank orders of the potency of the anesthetics in animals parallel that of luciferase inhibition (West et al., 2014).

Franks and Lieb also reported that few anesthetics exist as stereoisomers and the effects of isomers can differ. When the stereoisomers are induced into a lipid substrate, the physical effects on the lipid are similar. The anesthetic is acted as a stereoselective "receptor" and would implicate a protein as the site of action. At Mihic et al. (1997) study to reconcile the apparent problem of the nonspecific action of anesthetics on a wide range of protein channels including glycine, glutamate, GABA, and other neurotransmitter-activated channels.

2.3 Inhalant Anesthetic Pharmacokinetics

An anesthetic gas movement will start from a series of partial pressure gradients, beginning at the vaporizer, continuing in the anesthetic breathing circuit, the airways, alveoli, blood, and ending in the tissues (West et al., 2014). Until equal partial pressures are developed throughout the system, the movement of that gas will sustain. As the lung act as a point of entry and exit of anesthetics gas to the body, the alveolar partial pressure controls the partial pressure of the anesthetic in all body tissues. Some factors like solubility, cardiac output, and the alveolar-to-venous anesthetic gradient are used to determine the uptake of the anesthetic agents from the alveoli into the blood. For example, the blood/gas partition coefficient of isoflurane is approximately 1.4 (Steffey and Mama, 2007). That indicates if the gas partial pressures are in equilibrium, the concentration in the blood will be 1.4 times greater than the concentration in the alveoli. A higher blood/gas partition coefficient means greater uptake of the gas into the blood.

Increased cardiac output presents the alveoli to more blood per unit time. The large volume of blood transfers more inhalant anesthetic from the alveoli, consequently lowering the alveolar partial pressure. Hence, a high cardiac output generally prolongs induction time. The anesthetic agent might be distributed faster within the body, but the arterial partial pressure blood is lower. This will take more time for the gas to attain equilibrium between the alveoli and the brain (West et al., 2014).

The brain/blood coefficient of isoflurane is 2.7; consequently, when the process reaches at equilibrium the concentration in the brain will be 2.7 times higher than the concentration in the blood (Steffey and Mama, 2007). All contemporaneous inhalation anesthetics have elevated adipose/blood partition coefficients. High adipose/blood partition coefficients mean that the maximum of the gas will accumulate in adipose tissue. In adipose tissue, the partial pressure of the gas rises very slowly since this tissue has a high capacity. Obese patients may take more time for awakening due to the store of inhalation anesthetics at the end of long periods of anesthesia (West et al., 2014). Luckily, adipose tissue has a comparatively low blood flow and does not accumulate effective amounts of anesthetic during the low periods of anesthesia.

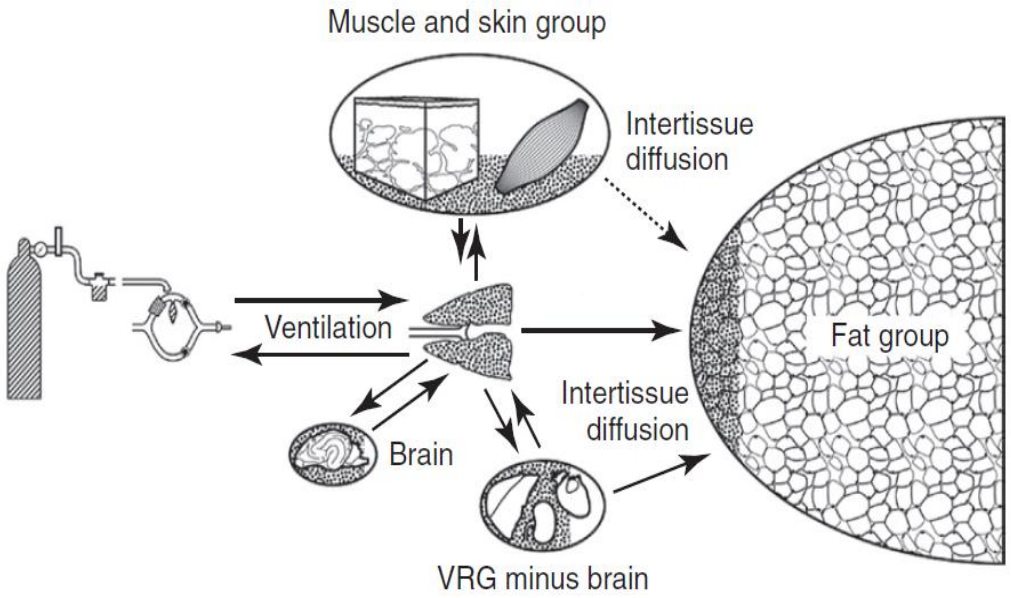


Figure 1: Anesthetic delivery to tissues is dependent on blood flow. Lung, brain, heart, and major organs (liver, kidney) have a relatively high blood flow compared with muscle and fat and are more susceptible to anesthetic drug-related effects.

2.4 Elimination of Inhaled Anesthetics

Elimination of inhalation anesthetics depends on ventilation, cardiac output, and solubility of the gas in blood and tissue (West et al., 2014). Due to differences in tissue solubility the rate of induction and recovery from anesthesia with inhalant anesthetics are differs between agents. The partial pressures in all tissue during induction are zero. But in recovery, the partial pressures of anesthetic are different in different tissues in the body which is controlled by the tissue anesthetic content and not the alveolar partial pressure (West et al., 2014). Elimination of anesthetics occurs during recovery due to exhalation and biotransformation. Some enzymes are responsible for inhalant anesthetic metabolism that is mainly located in the liver and kidneys. Anesthetic elimination via metabolism is approximately 50% for methoxyflurane, 10–20% for halothane, 5–8% for sevoflurane, 2.5% for enflurane, about 0.2% for isoflurane, 0.001% for desflurane, and nearly zero for nitrous oxide (Steffey and Mama, 2007).

The solubility of the anesthetic agent act as a major influence on the rate of induction and recovery. Anesthetic Agents with high blood/gas solubility might be partitioned into the blood to a greater extent than agents with low blood/gas solubility. Anesthetics with low blood/gas solubility do not divide into the blood to the extent, thus partial pressure is reduced fastly and recovery time is deceased. Whereas, highly soluble anesthetic agents have high blood concentrations, and will take a longer time to decrease the partial pressure if all other factors are remained equal (West et al., 2014).

2.5 General Pharmacological Actions of Inhalant Anesthetics

2.5.1 Central Nervous System

All volatile anesthetics change consciousness, memory, and pain perception by acting on the central nervous system. Most volatile anesthetics decreased the cerebral metabolic requirement for oxygen (CMRO2) mild to moderate and they usually have minimal effects on cerebral blood flow autoregulation at low MAC multiples (Mielck et al., 1998, 1999). Nitrous oxide may cause an increase in CMRO2, for that patient with intracranial hypertension should not be anesthetized (Algotsson et al., 1992; Hoffman et al., 1995; Roald et al., 1991). Halothane has significant effects on cerebral

blood flow autoregulation, it is a poor choice of anesthesia (Steffey and Mama, 2007). For that isoflurane, desflurane and sevoflurane are the inhalants of option at this time.

2.5.2 Cardiovascular System

Most inhalant anesthetic agents cause direct myocardial depression. Halothane causes dose-dependent bradycardia and depression of arterial blood pressure, generally has the fewest effects on vascular resistance (Steffey and Mama, 2007). Isoflurane, enflurane, sevoflurane, and desflurane cause some degree of vasodilatation, maintain tissue perfusions.

2.5.3 Respiratory System

All inhalation anesthetics tend to suppress the chemoreceptor reaction to carbon dioxide guidance to an accumulation of carbon dioxide and respiratory acidosis unless ventilation is assisted or controlled. The ether derivatives tend to be the greater supressant. Most inhalant agents may interfere with hypoxic pulmonary vasoconstriction and may worsen ventilation–perfusion matching in the lung (West et al., 2014).

2.5.4 Genital–Renal Systems

Most anesthetics decrease renal perfusions and increase antidiuretic hormone (ADH) secretion (Muir et al., 2013).Whereas in anuric renal failure patients inhalant anesthetics might be the safest anesthetic techniques as pulmonary excretion is not dependent upon renal function. Postpartum uterine bleeding may be incrreased due to inhalant anesthetics. Anestetics like desflurane, isoflurane, sevoflurane and nitrous oxide have been advocated for use because of the fast onset and termination of effect, and the transient effects on the delivered fetuses during caesarian section. Methoxyflurane and halothane are less desirable due to their greater solubility and slower elimination (West et al., 2014).

2.6 Halothane

Halothane has been used for several decades and is still a valuable anesthetic in many clinical practices. It was a chief advancement in inhalant anesthesia in its day. The chemical structure of halothane is 2-bromo-2-chloro-1,1,1-trifluoroethane, was first introduced into medical and to veterinary anaesthesia in 1956 (Hall, 1957). By

Sweking in 1951 after improvement for human anaesthesia, halothane was foremost used in veterinary anaesthesia in 1956, (Suckling, 1957). It was so enormously superior to existing agents that used throughout the world. Halothane was used extensively in human anesthesia until it appears potentially fatal effects associated with its use. In Daghfous et al. (2003) and Neuberger (1998) study recorded, human patients developed a syndrome known as halothane hepatitis. The guinea pig is particularly susceptible (Lunam et al., 1985) and in goats some reports of postanaesthetic fatalities associated with acute liver damage (Antognini and Eisele, 1993). Halothane was the first inhalation agent that would be effectively used in both large and small animals. Although halothane has no longer 'authorized' in North America or Europe for medical or veterinary use, but still used in other parts of the world, and also remains on the World Health Organisation's list of core medicines (WHO, 2010).

2.6.1 Physical - chemical properties of halothane

Halothane is a colourless liquid, which is broken down by ultraviolet light and so it can be stored in dark bottles with thymol as a preservative, that does not volatilize to the same degree as halothane. Due to thymol a sticky residue collects inside in the calibrated vaporizers, that decreasing anaesthetic output and should be cleaned out during periodic maintenance (Hall and Clarke, 2014). It has a characteristic odor like chloroform and sweet, burning taste. It is slightly liquefiable in water and miscible with alcohol. At 20°C, halothane's specific gravity is 1.872–1.877 and vapor pressure is 243 mmHg.

Chemically, halothane is classified as a halogenated hydrocarbon, but chemically it is not related to the ethers (West et al., 2014). Halothane is non-explosive and relatively stable anesthetics and low blood-gas solubility coefficient: 2.54. relative to ether which is most used prior to halothane, that means it provides smooth and rapid induction and recovery from anaesthesia and the incidence of postoperative nausea and vomiting is low and relatively less toxic than previously used inhalant anaesthetic agents. Halothane can be used in a closed-circuit system and does not react with soda lime. Halothane relatively safety, potency, controllability, non-flammability, and comparatively low cost. Minimal Alveolar Concentration (MAC; %) in oxygen reported for halothane in various species: Dog = 0.76; Cat = 0.82; Horse = 0.88; Human = 0.76 (Plumb and Pharm, 2011).

2.6.2 Pharmacokinetics

The maximum part of halothane is rapidly absorbed through the lungs (Muir et al., 2013). About 12% of the absorbed drug is metabolized through the liver and formed trifluoroacetic acid (only small amounts), chlorine, and bromine radicals which are excreted in the urine (West et al., 2014). The mass of the absorbed drug is re-excreted through lungs and dispelled with expired air.

2.6.3 Effects on different organs and systems

2.6.3.1 Nervous and musculoskeletal system

Halothane causes dose-dependent depression of the CNS and increases cerebral blood flow with analgesics During light anesthesia muscle relaxation is moderate and is a poor analgesic and does not contribute to postoperative analgesia, so preemptive analgesic supplementation is very effective (Hall and Clarke, 2014). It causes malignant hyperthermia can be triggered in susceptible people, swine, dogs, and cats a genetic muscle defect (Muir et al., 2013).

2.6.3.2 Respiratory system

Halothane induces dose-related respiratory depression, leading to a progressive increase in PaCO2. Nevertheless, under halothane anaesthesia animals tend to breathe spontaneously better than the more modern agents (Steffey, 2002). It does not irritate the respiratory mucosa in contrast to isoflurane, it can be used for induction of anaesthesia without causing breath-holding (Hall and Clarke, 2014).

2.6.3.3 Cardiovascular system

Halothane causes dose-dependent bradycardia and depression of arterial blood pressure in all mammalian species at clinical concentrations due to a negative inotropic effect, although it causes a little block of transmission at sympathetic ganglia. Bradycardia is common due to vagal activity (Muir et al., 2013). It can cause hypotension that is related to the depth of anesthesia and at low concentrations decrease in myocardial contractile performance and vasodilatation at high concentrations (Muir et al., 2013). Halothane sensitizes the heart to catecholamine-induced tachyarrhythmias. Cardiac arrhythmias are related to CO2 accumulation, hypoxia, catecholamine release. (Steffey et al., 1987; Dunlop et al., 1987). Due to

increased systemic vascular resistance at the start of surgery blood pressure tends to increase (Wagner et al., 1995).

2.6.3.4 Reproductive system

Halothane has teratogenic effects and crosses the placental barrier. These anesthetics have potential risks in canine and feline pregnancy (Papich, 1992).

2.6.4 Precautions

The patients with malignant hyperthermia or patients with hepatic function impairment halothane is contraindicated. It is also contraindicated in patients with cardiac arrhythmias, increased CSF or head injury, myasthenia gravis, or pheochromocytoma (cardiac arrhythmias due to catecholamines) (Muir et al., 2013).

2.7 Isoflurane

Isoflurane, it is a structural isomer of enflurane, and present as a racemic mixture of two optical isomers Stevens (1972). Isoflurane is successfully authorized as an anaesthetic agent to induce and to maintain anaesthesia in many species and has a 'minimal residual limit' for use in food animals in Europe. Over 40 years, it has been used widely in humans. Widespread reconsideration of its pharmacological property are those of Wade and Stevens (1981) and Eger (1984). In small animals, isoflurane can be used satisfactorily in vaporizers in the 'in circle' method (Brosnan et al., 1998)

2.7.1 Physical - chemical properties of isoflurane

Isoflurane is a colorless, non-flammable, stable liquid supplied in dark coloured glass bottles which is a tight, light-resistant container, mildly pungent musty, ethereal odor and does not require the use of any preservative. At 20°C, the specific gravity of isoflurane is 1.496 and vapor pressure is 238 mm Hg. Its boiling point is 48.5°C and solubility coefficients are blood-gas: 1.4; and oil-gas: 91(Plumb and Pharm, 2011). Isoflurane should be stored at room temperature; it is comparatively unaffected by exposure to light. Isoflurane can react with dry soda lime to produce carbon monoxide (Kharasch, 2008). Isoflurane is high volatilite and low solubility in blood and tissues that means it provides rapid induction and recovery from anaesthesia. Isoflurane is irritant to the airways, causing airway secretions, coughing and breath-holding, not

suitable for ‘mask’ induction (Hall and Clarke, 2014). Minimal Alveolar Concentration (MAC%) in oxygen recorded for isoflurane in various species: Dog = 1.5; Cat = 1.2; Horse = 1.31; Human = 1.2. Several factors may alter MAC (acid/base status, temperature, other CNS depressants on board, age, ongoing acute disease, etc) (Plumb and Pharm, 2011).

2.7.2 Pharmacokinetics

Maximum part of isoflurane is rapidly absorbed through the lungs alveoli. It is quickly delivered into the CNS and crosses the placenta. About 0.17% of absorbed drug is metabolized through the liver and only very small amounts of inorganic fluoride are formed. The vast of the absorbed drug is re excreted by the lungs (Muir et al., 2013)

2.7.3 Effects on different organs and systems

2.7.3.1 Nervous system

Isoflurane produces generalized, dose-dependent CNS depression. If normal ventilation is maintained, cerebral blood flow is not increased. Isoflurane, at 1 MAC or less can preserve cerebral vasculature response to CO2 and can decrease cerebral vascular resistance and cerebral metabolic rate (Young, 1992).

2.7.3.2 Respiratory system

Isoflurane Produces clinically significant respiratory depression. Initially increase the tidal volume with the depth of anesthesia Decreased respiratory rate causes to increase hypoventilation (increased PaCO2) with time (Muir et al., 2013).

2.7.3.3 Cardiovascular system

Isoflurane can be used securely in patients with hepatic or renal disease and it has minimum myocardial depressant and catecholamine sensitizing effects. (Plumb and Pharm, 2011). Cardiovascular depression due to isoflurane is dose-related. Marked dose-dependent fall in arterial blood pressure and peripheral vascular resistance decreased with increasing depth of anesthesia. Initially, hypotension occurred due to vasodilatation but is augmented by decreased myocardial contractile performance when excessive inhalant anesthetic concentrations are delivered. The myocardium does not sensitize to catecholamine-induced arrhythmias by isoflurane. It induced little myocardial depression, cardiac output and blood flow remain good, and the heart

rate is well maintained. Cardiac contractility is depressed less than with halothane (Hall and Clarke, 2014).

2.7.3.4 Gastrointestinal system

Isoflurane decreased smooth muscle tone and motility. Due to minimal hepatic metabolism no hepatotoxicity is reported (Muir et al., 2013). GI effects (nausea, vomiting, and ileus) have been reported.

2.7.3.5 Renal system

Renal blood flow is dose-dependently and reversibly depressed (Muir et al., 2013).

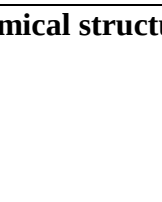
2.7.3.6 Reproductive system

Some animal studies have reported that isoflurane may be fetotoxic. During pregnancy, it should be used cautiously. These drugs seem to be safe in dogs and cat (Papich, 1992), if they are not administered when the animal is near term.

2.7.4 Precautions

Isoflurane is contraindicated in patients with malignant hyperthermia, increased CSF or head injury or myasthenia gravis. Isoflurane can be irritating to the respiratory system and not recommended for mask induction (Clarke, 2008).

Table 1: Physico-chemical properties of Halothane and Isoflurane. Modified from Steffey E.P. in Lumb & Jones' Veterinary Anesthesia. (2007).

Agent	**Halothane**	**Isoflurane**
Trade name	Halosin	Forane
Chemical structure		
Colour code	Red	Purple
Vapour pressure **at 20°c** **at 24°c**	243 mmHg 288 mmHg	240 mmHg 286 mmHg
% Metabolisation	20-25	0.17
Boiling point	50.2 °C	49 °C
Blood-gas partition coefficient **at 37°c**	2.54	1.46

2.8 Monitoring the anesthetized patient

During surgical process, the administration of anesthesia and monitoring of the patients is a complicated and need to multifaceted skill both knowledge and practice. The safety of the patient is dependent on awareness and response to potential problems of the anesthetist. This is the anesthetist's major responsibility to monitor the security of his/her patient at all times.

The anesthetized patient monitoring is a continuous process throughout the anesthetic period from pre-medication to full recovery. Vital signs and other monitoring parameters (muscle tone, eye position, pupillary reflex activity and status of surgical procedure) are recorded to the surgery record every 5 minutes throughout the procedure, but patient monitoring should be continuous. The anesthesiologist should be conscious of delicate changes in parameters and prepared to address any emergency issues.

2.8.1 Oxygen saturation (SpO_2)

Pulse oximeter is a simple continuous noninvasive assessment that provides real-time values of percentage of oxygenated hemoglobin in the arterial blood (SpO_2) and pulse rate (West et al. 2014) therefore, it helps the anesthetist to unroll hypoxemia in the patient before developing other clinical signs (Dorsch and Dorsch, 2008; Sinex, 1999). It is ideal for perioperative monitoring of the percentage of oxygenated hemoglobin in the arterial blood (SpO_2) (West et al., 2014). Normal oxygen saturation (SpO_2) in anesthetized patients is 95-100%.

The monitor assesses through differentiating the ratio of light absorption during pulsatile and non-pulsatile blood flow and give a pulse wave and a digital display of the percentage of oxygenated hemoglobin saturation in the arterial blood (SpO_2) (Faunt et al., 2011). A pulse oximeter reading of 90-95% indicates that the patient's hemoglobin is not fully saturated and a respiratory or cardiovascular problems may be present. The patient will not become hypoxic until the reading falls to 90% or less) (West et al., 2014).

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In McEwen et al. (2010) study, vasoconstriction and vasodilation of blood vessels presenting inaccurate SpO_2 readings. Low blood pressure may cause a less accurate pulse oximetry reading, via peripheral vasoconstriction the low pressure redirecting the blood flow to vital organs (Barton et al., 1996). In anesthetized patients, the SpO_2 values should be maintained above 95%; lower values indicate hypoxemia (West et al. 2014).

Göksen et al. (2009) study SpO_2 values were normal in dog during general anesthesia and no significant difference observed between the anesthetic groups due to a high inspired oxygen fraction. In water buffalos administration of 100% oxygen along with either halothane or isoflurane anesthesia led to higher values of SpO_2 observed in Bodh et al. (2014) study.

2.8.2 Respiratory rate, depth and character

The rate and depth can be monitored by observing the movement of the chest or reservoir bag. Thorax excursions should be count with both spontaneous respiration and assisted ventilation. Respiratory rate and character should be assessed via

esophageal stethoscope. The normal respiratory rate in anesthetized patients is 10-20 breaths/minute (rates up to 40 may be seen occasionally). The respiratory system functions depressed by all volatile anesthetic agents (Steffey and Mama, 2007). Inhalation anesthetics cause a dose-related respiratory depression in dogs (Juodzente et al., 2018).

The decrease RR sequel of hypoventilation with increasing EtCO2 mmHg (Doi et al., 1987, Mutoh et al., 1997). Halothane anesthesia causes least respiratory depression than other inhalant agents in the dog (Mutoh et al., 1995). Depth of anesthesia is related with the rate and tidal volume. When depth of anesthesia is increased, that causes decrease in both rate and tidal volume. When the animal feels hypoventilations, some alveoli cannot adequately inflate. These alveoli partially collapse, leading to atelectasis (partial collapse of lungs).

Hyperventilation act as an indicator that the CO2 is not being adequately expelled from the breathing circuit through the CO2 absorber. An increased respiratory rate may reveal an evolution from moderate to light anesthesia and is sometimes one of the first signs of arousal from anesthesia. With thoracic and diaphragmatic components, breathing should be smooth and regular. Difficult or labored breathing may indicate the presence of an airway obstruction (Muir et al., 2013).

In another study dog, undergoing sevoflurane, isoflurane and halothane anesthesia are causes a statistically significant decrease in respiratory rate (Polis et al., 2001). Göksen et al. (2009) and Mutoh et al. (1997) reported that ISO and HAL in dogs induced a RR depression. Halothane anesthesia causes a decrease in respiratory rates and depth in bulls was reported in (Greene et al., 1998) and cattle (Takase, 1976) study. In horses, Grosenbaugh and Muir (1998) study were reported a decrease in respiratory rate during isoflurane anesthesia. Higher respiratory rates were noticed during isoflurane anesthesia in water buffaloes (Bodh et al., 2014) and in sheep (Genccelep et al., 2004) which is similar to our study results.

2.8.3 Cardiovascular function

Inhalation anesthetics induce dose-dependent and drug-specific variations in the cardiovascular system and decrease cardiac output (CO). The sequel of all volatile

anesthetics on heart rate (HR) is variable and its effects depend on agent and species (Steffey and Mama, 2007). Among the coexisting agents in use, halothane depresses CO in animals (Steffey and Howland, 1978, Steffey and Howland, 1980). The decrease CO is due to a decrease in stroke volume and dose dependent depression for anesthetics in myocardial contractility (Warltier and Pagel, 1992, Paget et al., 1991).

HR is not significantly altered with halothane anesthesia other than isoflurane, desflurane, and sevoflurane anesthesia usually increased HR in humans (Malan et al., 1995 and Weiskopf et al., 1991). Halothane has dose-dependent the cardiovascular depressant effects, and increased dose causes a decrease of arterial blood pressure (Steffey and Mama, 2007). Volatile anesthetics increased HR when compared with conditions in awake, calm dogs (Paget et al., 1991 and Mutoh et al., 1997). In dogs in lack of other modifying factors (e.g., noxious stimulation) the HR usually remains stable over a range of alveolar concentrations (Bernard et al., 1990, Clarke et al., 1996, Klide, 1976).

Normal resting physiologic reference limits for heart rates in dogs range from 60–150 bpm (John and Phillip, 2011). Under general anaesthesia, the lowest acceptable heart rates are controversial and HR of <55-60 bpm in most dogs would be considered too slow, for large dogs 55 beats/min, and 65 beats/min should be higher in small breed dogs and heart rate is a major determinant of cardiac output (Hall and Clarke, 2014). Usually, dogs that received opioids and alpha-2 agonists drugs are faced bradycardia due to the effects of these drugs (Smith, 2016).

ISO causes an increased HR in dogs (Merin et al., 1991). In Paget et al., 1991study, little influence of HAL on HR in dogs, a slight increase was observed in dogs. Heart rate was increased with isoflurane and halothane anesthesia by concentration Picker et. al. (2001) study. In human Halothane depresses cardiac function without changing in peripheral resistance (Prys-Roberts et al., 1972, Merin and Basch, 1981, Sonntag et al., 1978), whereas isoflurane presumably conserves cardiac output, perhaps with an increase in sympathetic autonomic activity (Graves et al., 1974 and Wolf et al., 1986).

In Bodh et al. (2014) study, there was a significant decrease in heart rate in HAL group in water buffalos at. In a similar study, a decrease HR in lambs, and piglets

(Brett et al., 1987), piglets (Schieber et al., 1986), and an increase in HR in dogs (Frink et al., 1992), bulls (Greene et al., 1998) and horses (Steffey et al., 1987) were observed. Increase heart rate in ISO anesthesia was observed in cats (Hikasa et al., 1997) and goats (Hikasa et al., 1998). The changes in heart rate during maintenance of anesthesia might be due to few potential causes like level of anesthesia, differences in the amount of sympathetic stimulation within the anesthetics group (Bodh et al., 2014).

2.8.4 Arterial blood pressure

Measurement of arterial blood pressure reports information related with the adequacy of blood flow to the patient's tissue. All inhalation anesthetics induce a dose-dependent decrease in arterial blood pressure (Steffey et al., 1984; Mutoh et al., 1997; Steffey et al., 1974; Frink et al., 1992, Steffey and Howland, 1978). Decreased stroke volume and peripheral vascular resistance effects on to decrease blood pressure (Malan et al., 1995; Lowe et al., 1996; Mutoh et al., 1997). Systolic (SAP), mean (MAP), and diastolic (DAP) arterial pressures in awake healthy animals are approximately 125–160 mmHg, 90–110 mmHg, and 75–95 mmHg, respectively.

Arterial blood pressure is decreased when premedication like detomidine or medetomidine or anaesthesia ketamine or tiletamine has induced, it may decreased from the awake value during anaesthesia (Hall and Clarke, 2014). In mature animals MAP less than 65 mmHg is called hpotension. In dogs and cats, less than 60 mmHg MAP is allowed. During anaesthetized patients, MAP is not usually allowed less than 65–70 mmHg because it may increase risk for postanaesthetic myopathy.

In Juodzente et al. (2018) study, SAP and DAP were within the reference limits. A significant decrease was reported in MAP values during ISO anesthesia Göksen et al. (2009) study. MAP values were recorded lower with SEV and ISO anesthesia in comparison to HAL (Mutoh et al., 1995 and Frink et al., 1992). In another study, HAL anesthesia significantly decreased SBP, DBP, and MAP values in water buffalos Bodh et al. (2014). A similar hypotensive effect in cattle (Wolf et al., 1968) and buffaloes (Bose and Kohli 1983; Gahlawat et al., 1986) was reported in halothane anesthesia.

Halothane anesthesia causes a fall in arterial blood pressure and cardiac output in goats (Hikasa et al., 1998). Whereas isoflurane causes depression in arterial blood pressure and a smaller decrease in cardiac output in cats and dogs (Steffey et al., 1987; Bernard et al., 1990). During anesthesia hypotensive effect might be due to depression of myocardial contractility and decreased cardiac output (Stoelting, 1991). Excessive anesthetic depth is the most common cause of hypotension. Another causes are pre-operative dehydration, hypovolemia due to intra-operative bleeding or hypothermia or hypoxia. To overcome hypotensive effects in anesthetized patients, anesthetic depth should be reduced, need to increase the intravenous fluids administration or vasoactive drugs such as dopamine, dobutamine, or ephedrine can be used. If the patients keep in untreated conditions, it may causes cardiac arrest during anesthesia or neurological deficits, blindness or renal failure after recovery from anesthesia (Hall and Clarke, 2014).

2.8.5 Body Temperature

Anesthesia will typically lower the body temperature and can lead to hypothermia, which can result in prolonged recovery from anesthesia as well as other complications (Steffey and Mama, 2007). Small puppies and kittens are especially vulnerable. General anaesthesia inhibits thermoregulation, vasoconstriction, and shivering, thus inhibits generalized redistribution of body heat. When the temperature decreased below 32.8°C (91°F), life-threatening cardiovascular depression might have occurred Hall and Clarke (2014).

Peripheral vasodilator properties of inhalation anesthetics and their effects depressed on heat regulation (Bernard et al., 1990 and Topal, 2005). Decrease metabolic rate, reduced skeletal muscle tone, muscle relaxation along with the depression of the thermoregulatory center (Matsukawa et al., 1995) may be associated with to decrease in rectal temperature. The first 20 minutes of anesthesia the greatest loss in body heat occurs. Until the body temperature become normalized animals can be placed on a heating pad and covered with a blanket during recovery. It is needed to monitor body temperature continuously and supplemental of heat should be discontinued when the patient's temperature is 99-100℉.

HAL anesthesia causes hypothermia in buffaloes (Bodh et al., 2014). It was reported that during halothane anesthesia rectal temperature decreased significantly in adult water buffaloes (Malik, 2010). The blood gas solubility of inhaled anesthetics increased for hypothermia that causes anesthetics slow to saturate in the blood and tissues (Dohoo, 1990). In Ramachandra et al. (1989) study, halothane anesthesia caused decrease in body temperature in humans.

Chapter III

Materials and Methods

3.1 Study period

The present study was conducted from January 2019 to December 2019 at Shahidul Alam Quadery Teaching Veterinary Hospital (SAQTVH) & Teaching and Training Pet Hospital and Research Center (TTPHRC), Chattogram Veterinary and Animal Sciences University (CVASU), Chattogram Bangladesh.

3.2 Study area

The study was driven at SAQTVH & TTPHRC in Chattogram Veterinary and Animal Sciences University as case registered and outpatients of Chattogram Metropolitan area and Dhaka Metropolitan area.

Figure 2: Geographical location of SAQ Teaching Veterinary Hospital, Chattogram, CVASU.

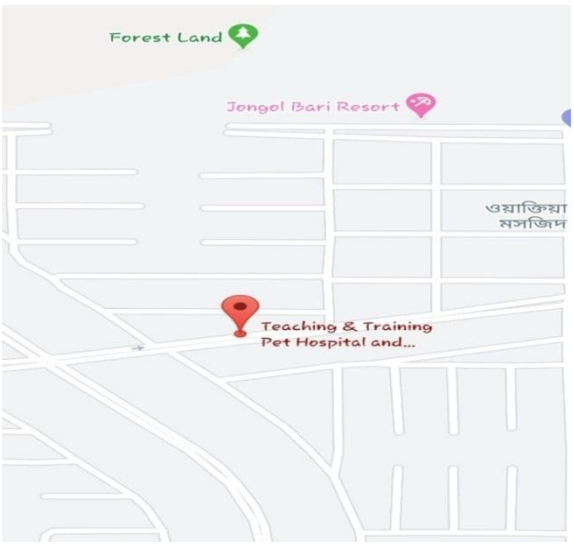


Figure 3: Geographical location of Teaching and Training Pet Hospital and Research Center, Dhaka, CVASU.

3.3 Study design

A total of fourteen (n=14) crossbreed dogs of both sexes weighing from 11 to 28 kg and age between 2 to 8 years were used in this experiment. A preoperative anamnesis was taken and a routine pre-anesthetic physical observation was performed on each patient. Total samples were randomly allocated into two groups (n = 7 in every group; Halothane Group & Isoflurane Group) for this study.

3.3.1 Preanesthetic procedures

Xylazine HCl @ 1 mg/kg was given intramuscularly (IM) 30 minutes before induction of anesthesia as a preanesthetic.

3.3.2 Fluid therapy

All dogs were administered 0.9% sodium chloride solution at a flow rate of 10 mL/kg/hr. through a 22-gauge catheter or 21 gauge butterfly needle placed in the left cephalic vein by using an infusion pump.

3.3.3 Anesthetic procedures

Induction of anesthesia was performed by using propofol @ 2 mg/kg intravenously over 50- 60 seconds. The onset of anesthesia was accomplished when the eyeball position was rotated down and absent of palpebral reflex (examined by lightly tapping the medial or lateral canthus of the eye and observing whether the animal blinks or not in response) and pedal (tested by pinching a digit and observing whether the animal flexes the leg and withdrawing the paw or not) reflexes and there were no jaw tone (assessed by attempting to open the jaws wide and estimating the amount of passive resistance).

3.3.4 Intubation

After the loss of the swallowing reflex and jaw tone, dogs were orally intubated with cuffed endotracheal tube (ET tube) according to body weight. Oxygen flow rate was maintained at 25 to 50 ml/kg/min.

3.3.5 Maintenance of anesthesia

A circle semi-open rebreathing anesthesia system was used throughout the study with a calibrated halothane (HAL) and isoflurane (ISO) vaporizer. For group A (n=7) anesthesia was maintained with halothane vaporizer for induction (3.5% to 4%) and group B (n=7) anesthesia was maintained with isoflurane vaporizer for induction (3% to 4%). HAL and ISO vaporizer setting was adjusted from 1.5% to 2.5% according to the depth of anesthesia. The dial of the vaporizers was progressively reduced or increased to the percentage required to maintain the plane of anesthesia according to a clinical response to the tail clamp, movements, and changes in heart rate (HR), respiratory rate (RR) and blood pressure. The entire study was finished after 60 minutes.

3.4 Measurements and monitoring:

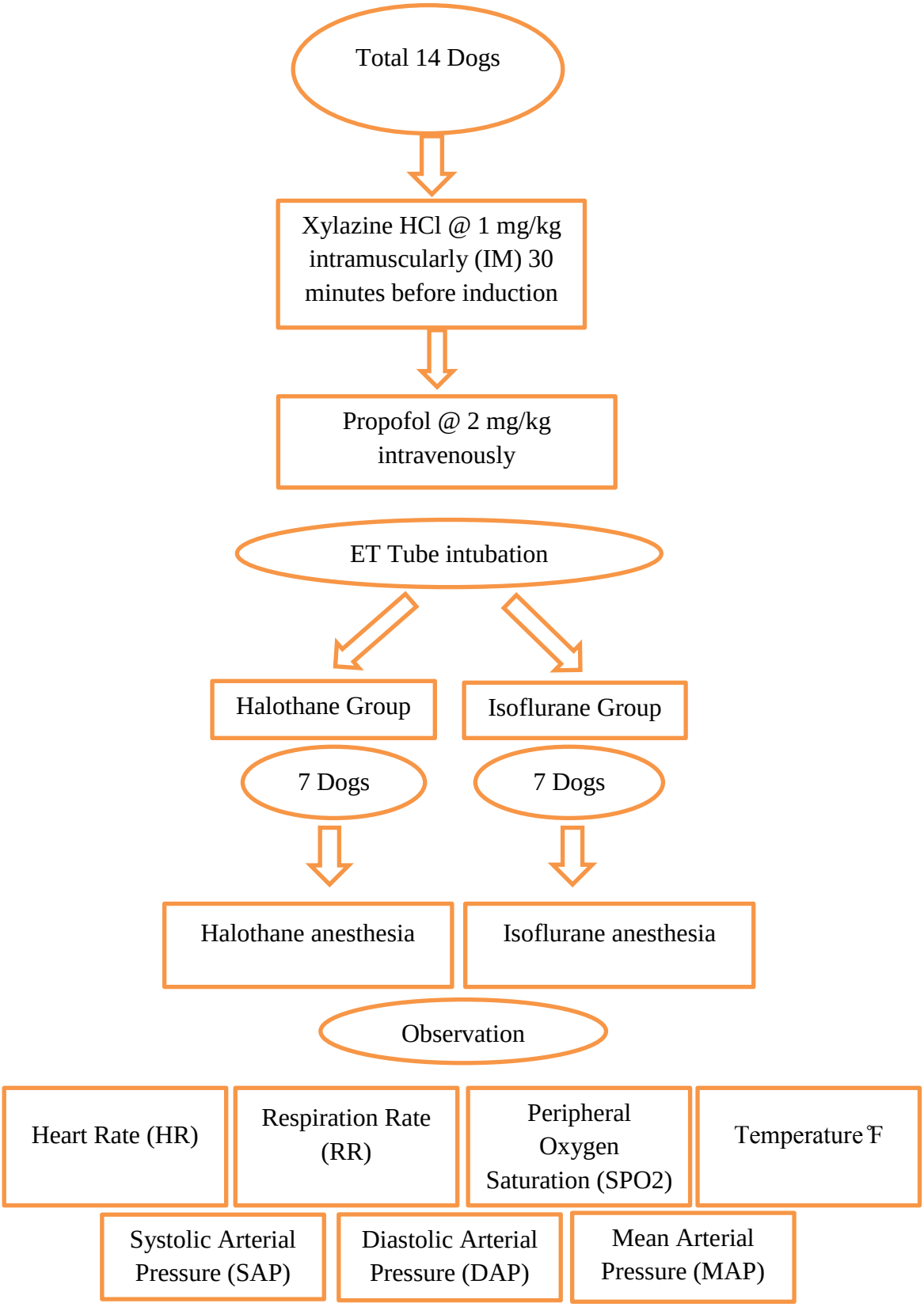
A pre-structured anesthesia record sheet was used for patient monitoring throughout the anesthesia period. Heart rate (HR), saturation of hemoglobin with oxygen (SpO_2), respiratory rate (RR), rectal temperature, noninvasive systolic (SAP), diastolic (DAP) and mean arterial blood pressures (MAP) were monitored using a veterinary patient monitoring system. Capillary refill time (CRT), reflexes (palpebral, pedal), jaw tone, and eye position (straight, down) were also assessed to determine the depth of anesthesia. The first measurement of parameters was taken at one min after the loss of consciousness with HAL or ISO and the others were recorded every 5 minutes interval up to the completion of the study (60 min).

Rectal temperature was measured using an electric thermometer probe placed into the rectal mucosa. HR and RR were monitored by placing the electrodes at the level of the right and left elbows and the left patella and also ventral abdomen skin. Systolic and diastolic arterial blood pressures were measured by using standard oscillometry blood pressure measurement. The cuff was placed on the left antebrachium. SpO_2 was measured by a pulse oximeter (with the infrared sensor probe placed on the dog's tongue). A warm heating pad was used to maintain the temperature between 101℉ and102.5℉. The dogs were extubated when they were awake from anesthesia and the swallowing reflex appeared.

3.5 Statistical analysis:

To compare the cardiopulmonary parameters with each inhalation anesthetics group, all complied data were imported in Microsoft Excel- 2010 and transferred to STATA 13.0 version for statistical analysis. All data were expressed as mean ± standard error (SE). Descriptive statistics of general parameters like – temperature, HR, RR, SpO_2, SAP, DAP and MAP were analyzed by using paired t-test ($p \leq 0.1$) to determine the significance.

Schematic diagram of the research



Anesthetic procedure and patient monitoring during anesthesia

Figure 4: Intubation in dog

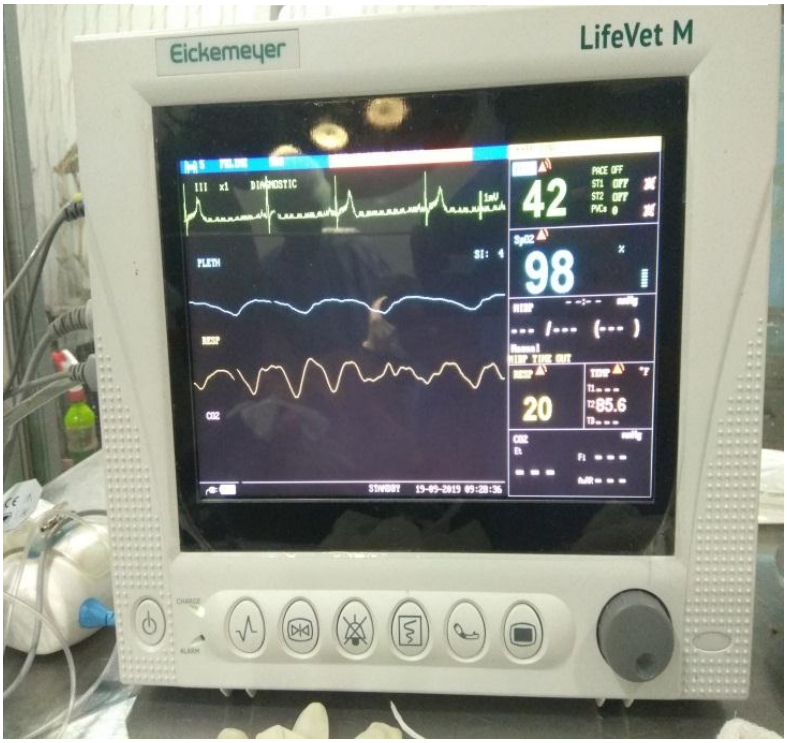


Figure 5: Monitoring the vital signs on monitor (Temperature, RR, HR, SpO_2, SAP, MAP, DAP)

Figure 6: Maintenance of anesthesia in dog using halothane.

Figure 7: Maintenance of anesthesia in dog using Isoflurane.

Figure 8: Monitoring of patient using Halothane anesthesia during docking in a German Shepard at CVASU.

Figure 9: Monitoring of patient using Isoflurane anesthesia during castration in a Lhasa Apso at TTPHRC.

Chapter IV

Results

The measurements of the cardiopulmonary parameters of the dogs in each anesthesia group were recorded after induction of anesthesia (0 min) to completion of the surgery for every 5 minutes interval.

4.1 Measurements of Body Temperature

Body temperature decreased gradually in both groups during the 15, 30, 45 and 55 minutes when compared to the first measurement values. But there was no significant difference in body temperature between the HAL and ISO groups ($p>0.1$) (Figure 10).

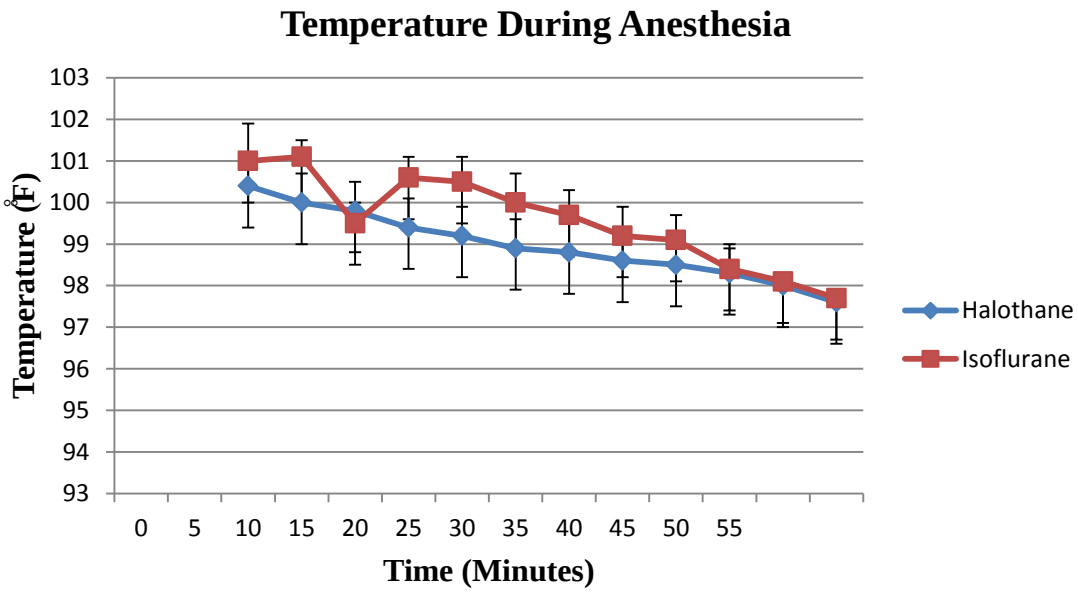


Figure 10: Values of temperature (F) during halothane and isoflurane maintenance anesthesia in dogs. Each point and vertical bar represents the mean±SE (n=7).

4.2 Measurements of Heart rate (HR)

There was no significant difference in HR between the anesthetic groups ($p>0.1$). HR did not significantly change when compared with the different anesthetic times ($p\geq0.1$) except 25 minutes of anesthesia period (Figure 11).

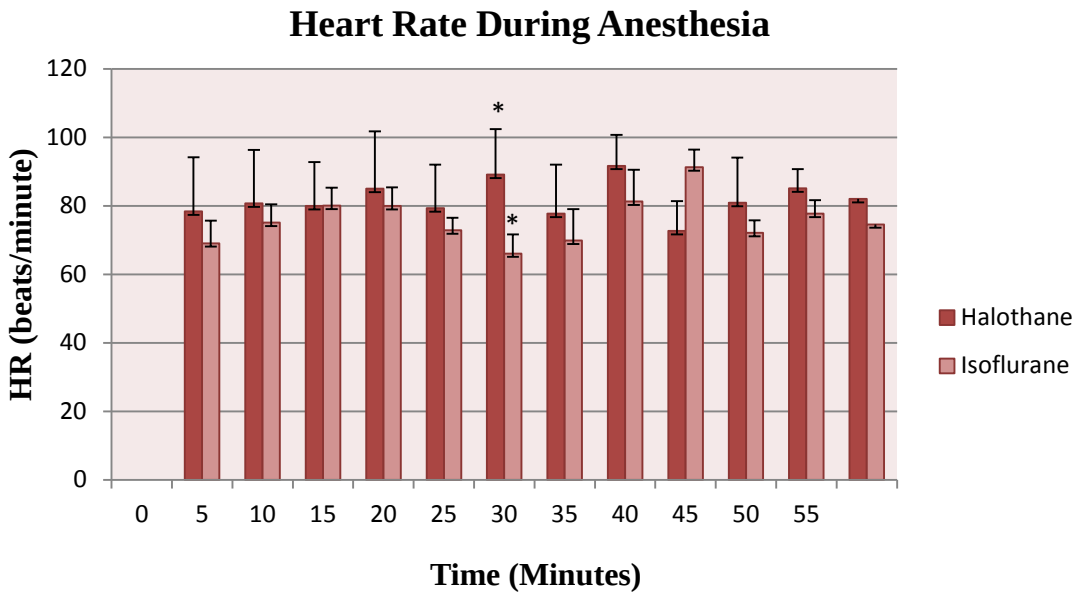


Figure 11: Values of heart rate (HR) during halothane and isoflurane maintenance anesthesia in dogs. Each point and vertical bar represents the mean±SE (n=7).

*: Significantly different between HAL and ISO group at corresponding interval ($p\leq0.1$)

4.3 Measurements of Respiratory rate (RR)

Isoflurane caused a significant increase in respiratory rate when compared with the halothane anesthesia group ($p \leq 0.1$). There was a significant increase of RR in ISO anesthesia when compared with different anesthetics times at 0, 10, 15, 20, 25, 30 35 min of maintenance of HAL anesthesia ($p \leq 0.1$) (Figure 12).

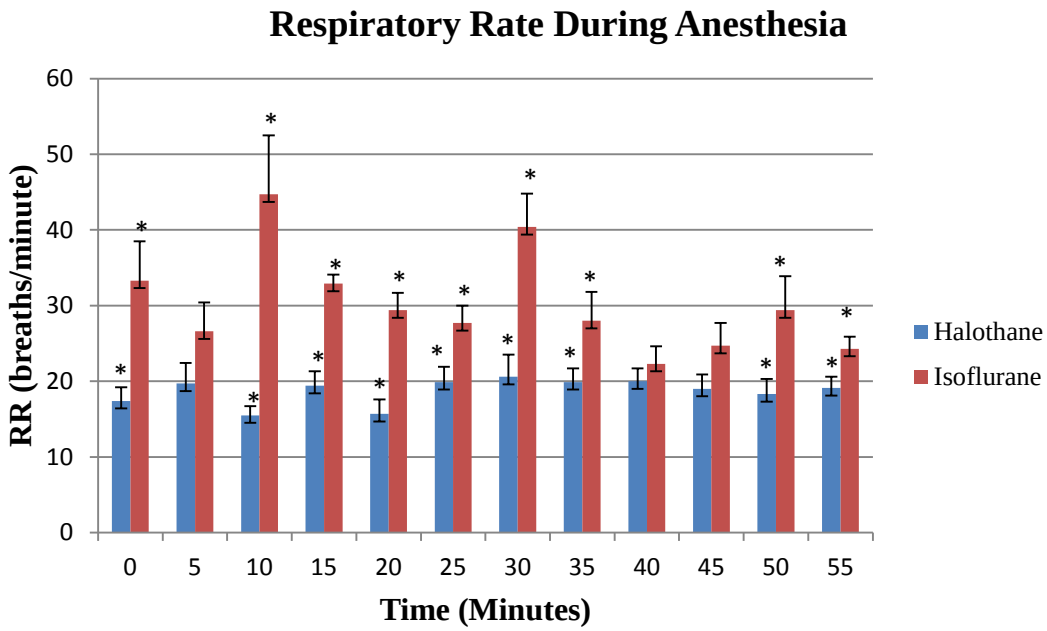


Figure 12: Values of respiratory rate (RR) during halothane and isoflurane maintenance anesthesia in dogs. Each point and vertical bar represents the mean±SE (n=7).

*: Significantly different between HAL and ISO group at corresponding interval ($p \leq 0.1$)

4.4 Measurements of Oxygen saturation (SpO_2)

In this study, all data were expressed as mean±SE. No significant difference was found between HAL and ISO groups in SPO_2 ($p>0.1$). Time had no significant influences on the SPO_2 value in different anesthetics times ($p>0.1$) (Figure 13).

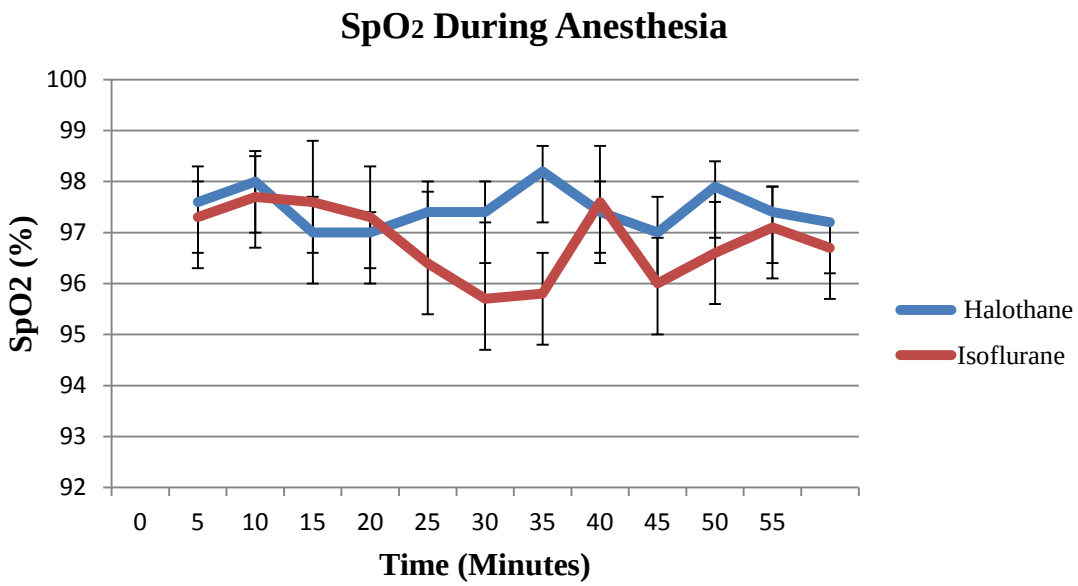


Figure 13. Values of Oxygen saturation (SpO_2) during halothane and isoflurane maintenance anesthesia in dogs. Each point and vertical bar represents the mean±SE (n=7).

4.5 Measurements of Arterial blood pressure

The mean±SE value of Systolic (SAP), diastolic (DAP), and mean (MAP) arterial pressures in 14 dogs are presented in figure 14, 15 & 16 respectively.

4.5.1 Systolic arterial pressures (SAP)

There was no significant difference between HAL and ISO groups in SAP ($p>0.1$) (Figure 14).

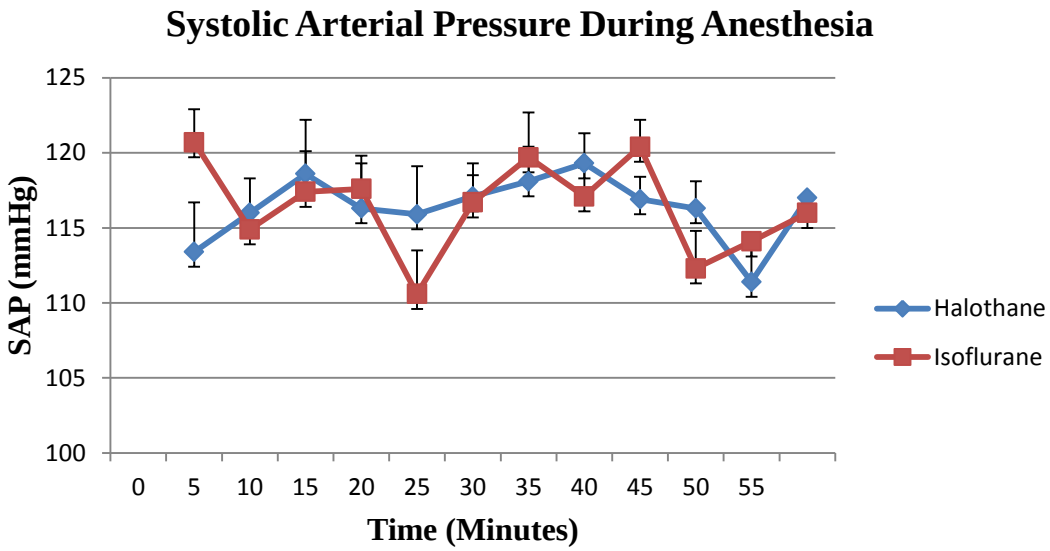


Figure 14: Values of systolic arterial pressure (SAP) during halothane and isoflurane maintenance anesthesia in dogs. Each point and vertical bar represents the mean±SE (n=7).

4.5.2 Diastolic arterial pressures (DAP)

In DAP value no significant difference was found in HAL and ISO groups. But time had a significant difference at the beginning of the anesthesia time, 10 and 35 min of maintenance of anesthesia period and when p value was (p=0.1, p= 0.09, p= 0.1) respectively (Figure 15).

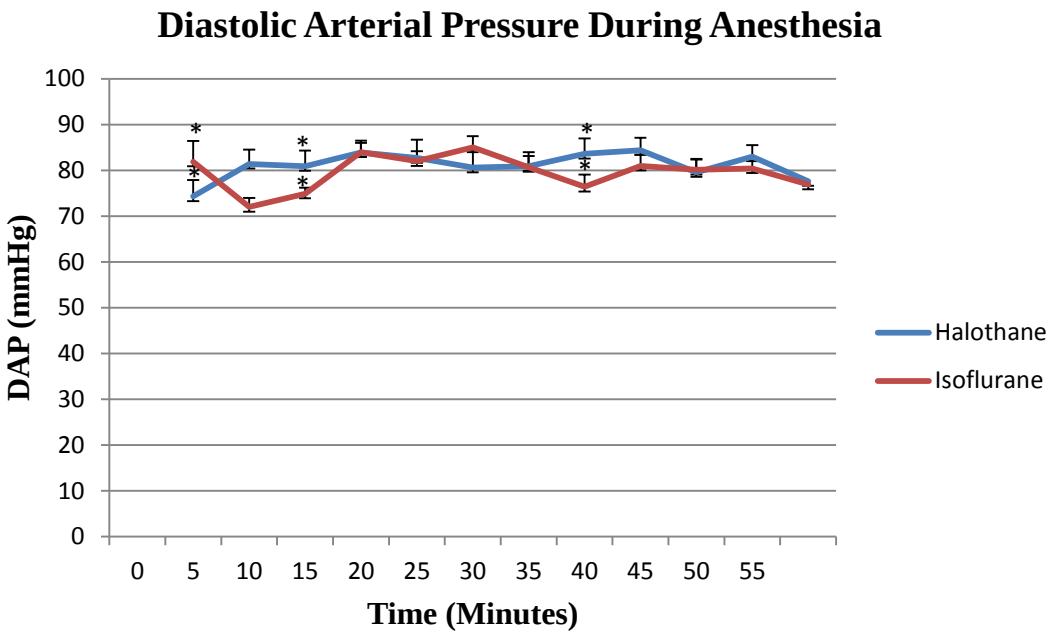


Figure 15: Values of diastolic arterial pressure (DAP) during halothane and isoflurane maintenance anesthesia in dogs. Each point and vertical bar represents the mean±SE (n=7).

*: Significantly different between HAL and ISO group at corresponding interval ($p \leq 0.1$)

4.5.3 Mean arterial pressures (MAP)

There was a significant difference documented at the beginning of anesthesia and 30 min of the maintenance of anesthesia ($p \leq 0.1$) (Figure 16).

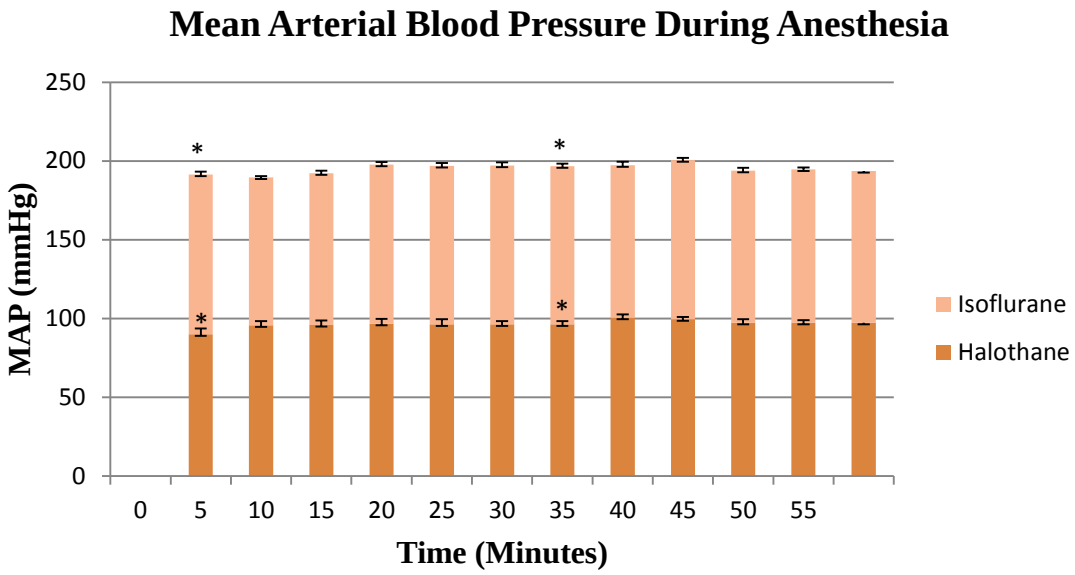


Figure 16: Values of mean arterial pressure (MAP) during halothane and isoflurane maintenance anesthesia in dogs. Each point and vertical bar represents the mean±SE (n=7).

*: Significantly different between HAL and ISO group at corresponding interval ($p \leq 0.1$).

Chapter V

Discussion

Inhalation anesthetics are used extensively for the anesthetic management of animals because of their rapid induction, rapid recovery with better control over the depth and duration of anesthesia (Stewart et al., 2003). In this study, we found both inhalation anesthetics to be safe and reliable for use in dogs. Inhalation anesthesia induces a dose-related cardiopulmonary depression in all animals (Polish, 2001). Halogenated anesthetics, like halothane and isoflurane, can change the cardiac rate and rhythm (Nakaigawa et al., 1995).

Both anesthesia groups cause a fall of the body temperature below the physiological limits. Time had influence on body temperature and significantly decreased during HAL and ISO anesthesia. This condition may be explained due to peripheral vasodilator properties of inhalation anesthetics and their effects depressed on heat regulation (Bernard et al., 1990 and Topal, 2005). Skeletal muscle tone decreased when metabolic rate reduced, muscle relaxation also decreased along with the depression of the thermoregulatory center occurred (Matsukawa et al., 1995) may be related with reduce rectal temperature in both the groups. Within the first 20 minutes of anesthesia the greatest loss in body heat occurs. HAL anesthesia causes hypothermia in buffaloes (Bodh et al., 2014). Rectal temperature significantly decreased during halothane anesthesia was reported in adult water buffaloes (Malik, 2010). The blood gas solubility of inhaled anesthetics increased for hypothermia that causes anesthetics to slow to saturate in the blood and tissues (Dohoo, 1990). In a similar study, halothane caused a decrease in body temperature in humans anesthesia (Ramachandra et al., 1989).

The mean HR was lower in ISO anesthesia group compared to HAL anesthesia at 0, 25 and 30 min but was still within the reference limits in our study. The effect of both anesthetics on the heart rate was examined, the difference between them was not significant ($p>0.1$). HR did not significantly change when compared with the different anesthetic times ($p\geq0.1$). In our study, under general anesthesia we managed to maintain HR within the physiological limits but our study results not supported to Göksen et al. (2009) study where during HAL anesthesia heart rate was lower

compare to during ISO and SEV anesthesia. ISO causes an increased HR in dogs (Merin et al., 1991). In another study, little influence of HAL on HR in dogs, a slight increase was observed in dogs (Pagel et al., 1991). Heart rate was increased with isoflurane and halothane anesthesia by anesthetics concentration (Picker et al., 2001). In human, Halothane depresses cardiac function without changing in peripheral resistance (Prys-Roberts et al., 1972; Merin and Basch, 1981; Sonntag et al., 1978), whereas isoflurane presumably conserves cardiac output, perhaps with an increase in sympathetic autonomic activity (Graves et al., 1974 and Wolf et al., 1986). There was a significant decrease in the heart rate in HAL group than ISO group in water buffalos at Bodh et al. (2014) study. In a similar study, a decrease HR in lambs, and piglets (Brett et al., 1987), piglets (Schieber et al., 1986), and an increase in HR in dogs (Frink et al., 1992), bulls (Greene et al., 1998) and horses (Steffey et al., 1987) were observed. It has been reported (Steffey and Howland, 1977) study in dogs that with an increase in alveolar volatile anesthetic concentration heart rate either remains constant or increases and an increase in anesthetic depth decreases heart rate due to increased vagal tone (Hall and Clarke, 1983). Increase heart rate in ISO anesthesia was observed in cats (Hikasa et al., 1997) and goats (Hikasa et al., 1998). The changes in heart rate during maintenance of anesthesia might be due to few potential causes like level of anesthesia, differences in the amount of sympathetic stimulation within the anesthetics group Bodh et al. (2014).

In this study, the respiratory rate showed a statistically significant increase ($P \leq 0.1$) at the 10^{th} to 35^{th} min of anesthesia in the isoflurane group. These increases cross the physiological limits (10 to 20 breathe/min) (Hall and Clarke, 2014). Hyperventilation act as an indicator that the CO2 is not being adequately expelled from the breathing circuit through the CO2 absorber and an elevated respiratory rate may indicate a progression from moderate to light anesthesia and is often one of the first signs of arousal from anesthesia (Muir et al., 2013). The respiratory rate did not change significantly in the group receiving halothane anesthesia and the recorded data were within the physiological limit. Halothane anesthesia causes least respiratory depression than other inhalant agents in the dog (Mutoh et al., 1995). The function of the respiratory system depressed by all volatile anesthetic agents (Steffey and Mama, 2007). Inhalation anesthetics cause dose-related respiratory depression in dogs (Juodzente et al., 2018). In Sen and Kilic (2018) study at the 15th min of propofol-

isoflurane anesthesia causes a statistically significant decrease ($P < 0.001$) of respiratory rate not supported our study, because in our study we reported increased respiratory rate. In another study dogs undergoing sevoflurane, isoflurane and halothane anesthesia are cause a statistically significant decrease in the respiratory rate ($P < 0.05$) (Polis et. al., 2001). Halothane anesthesia causes a decrease in respiratory rates and depth in bulls was reported in (Greene et al., 1998) cattle (Takase, 1976) study. In horses, (Grosenbaugh and Muir, 1998) study was reported a similar decrease in the respiratory rate during isoflurane anesthesia. The higher respiratory rate was noticed during isoflurane anesthesia in water buffaloes Bodh et al., 2014 and in sheep (Genccelep et al., 2004) which is similar to our study results.

In our study, we managed to maintain SpO_2 values within the reference limits (95-100%) during general anesthesia (West et al., 2014). No significant difference found in SpO_2 values ($p>0.1$) between HAL and ISO anesthesia group might be due to the anesthetic-induced depression occurred of central respiratory center and ventilation/perfusion of oxygenation take place in the lungs properly during general anesthesia in both group. Time had no significant influences on the SPO_2 values in different anesthetics times ($p>0.1$). Due to a high inspired oxygen fraction SpO_2 values were normal during general anesthesia and no significant different noticed between the anesthetic groups in Göksen et al. (2009) study. However, administration of 100% oxygen along with either halothane or isoflurane anesthesia led to higher values of SpO_2 in water buffalos observed by Bodh et al. (2014). Sen and Kilic (2018) showed that a peripheral oxygen saturation (SpO_2) was decreased significantly during anesthesia which was not supported our study because during general anesthesia SpO_2 values were within the reference limits.

In our study, no significant difference was found between HAL and ISO groups in SAP and DAP value ($p>0.1$). But time had a significant difference at the beginning of the anesthesia time, 10 and 35 min of maintenance of anesthesia period ($p=0.1$, $p= 0.09$, $p= 0.1$) in case of DAP, but was still within the physiological limits. The significant difference was documented in MAP at the beginning of surgery and 30 min of the maintenance of both anesthesia groups ($p\leq0.1$) within the physiological limit. Juodzente et al. (2018) said that SAP and DAP were within the reference limits which were supported by our study. A significant decrease was reported in MAP

values during ISO anesthesia Göksen et al. (2009) which was conflicts with our study because we documented significant difference in MAP but it was within the physiological limits. MAP values were recorded lower with SEV and ISO anesthesia in comparison to HAL (Mutoh et al., 1995 and Frink et al., 1992). In another study, HAL anesthesia significantly decreased SAP, DAP, and MAP values in water buffalos Bodh et al. (2014). A similar hypotensive effect in cattle (Wolf et al., 1968) and buffaloes (Bose and Kohli, 1983; Gahlawat et al., 1986) was reported in halothane anesthesia. Halothane anesthesia causes a fall in arterial blood pressure and cardiac output in goats (Hikasa et al., 1998). Whereas isoflurane causes depression in arterial blood pressure and a smaller decrease in cardiac output in cats and dogs (Steffey et al., 1987; Bernard et al., 1990). During anesthesia hypotensive effect might be due to depression of myocardial contractility and decreased in cardiac output (Stoelting, 1991). The most common cause of hypotension is the excessive anesthetic depth and other causes include hypovolemia due to intra-operative bleeding or pre-operative dehydration, hypothermia or hypoxia (Hall and Clarke, 2014). To overcome hypotensive effects in anesthetized patients, anesthetic depth should be reduced, need to increase the intravenous fluids administration or a vasoactive drug such as dopamine, dobutamine, or ephedrine can be used and if the patients keep in untreated conditions, it may cause cardiac arrest during anesthesia or neurological deficits, blindness or renal failure after recovery from anesthesia (Hall and Clarke, 2014).

From this study, we found a significant conclusion on the use of inhalation anesthetics during surgery. The present findings indicate that the respiratory effects of halothane were less suppressive than isoflurane anesthesia in dogs. On the cardiovascular system, there was no suppressive effect in dogs during surgery. A routine surgical treatment procedure, isoflurane and halothane ensure the stable plane of anesthesia with minimum side effects on the cardiovascular and respiratory systems. However, halothane and isoflurane both can be safely used in dogs.

Chapter VI

Conclusion

This research was conducted at Shahidul Alam Quadery Teaching Veterinary Hospital (SAQTVH) & Teaching and Training Pet Hospital and Research Center (TTPHRC), Chattogram Veterinary and Animal Sciences University (CVASU) Chattogram, Bangladesh from January 2019 to December 2019 to evaluate and compare the anesthetic effects of halothane and isoflurane anesthesia on certain cardiopulmonary parameters (Heart rate, respiratory rate, oxygen saturation, arterial blood pressure) along with anesthetic potency in dogs. The present findings indicate that the respiratory effects of halothane were less suppressive than isoflurane anesthesia in dogs. On the cardiovascular system, there was no suppressive effect in dogs during surgery. A routine surgical treatment procedure, isoflurane and halothane ensure the stable plane of anesthesia with minimum side effects on the cardiovascular and respiratory systems. However, halothane and isoflurane both can be safely used in dogs. Till now, the gaseous anesthesia is not popular for animal anesthesia in our country. Therefore the result of this research will be helpful to increase awareness of anesthetic management in anesthesia practices, improve the safety of canine anesthesia, and provide a foundation for further research in this area in Bangladesh.

Recommendations

With the progress of civilization, pet animal's population is increasing along with their popularity as a pet and also for research purposes in our country. Pet animal owners are much concerned about the health issue of their pet. During surgery, the pet owner demands a sound plane of anesthesia with a smooth recovery. Inhalation anesthetics play a major role to provide a stable work of the cardiovascular and respiratory systems with minimum side effects. From our study, we found a significant conclusion on use of inhalation anesthetics during surgery. Large sized population would provide a more specified result for better conclusion, however, the main limitations of the study were a small number of clinical patients were recorded, the lack of knowledge of the use of anesthetic machine and associated factors that affected the results of the study. Further detailed investigation of the use of inhalation anesthetics during surgery and effects of anesthetics on other cardiopulmonary parameters (e.g. end-tidal carbon dioxide level (ETCO2), the arterial partial pressure of oxygen (PaO2), the arterial partial pressure of carbon dioxide (PaCO2), arterial pH and larger sample sizes are recommended.

Chapter-VII

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Annex-I

A questionnaire for the dogs undergoing surgery with gaseous anesthesia.

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: Defication: Y/N
Urination: Y/N

F/H: Normal/Loss of Appetite/Off-fed/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:

Recovery:

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

Sternal recumbency……..min,

Standing **.....**……..min.

Immediate PO condition: quiet & 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

Biography

DR. Aparna Datta is the daughter of Pijush Kanti Datta and Archana Rani Datta. 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 in Teaching and Training Pet Hospital and Research Center of Chattogram Veterinary and Animal Sciences University. Her research and publications are based on veterinary surgery and anesthesiology. She has great interest on small animal anesthesiology.