# COMPARISON OF MAINTENANCE ANESTHESIA WITH PROPOFOL AND HALOTHANE COMBINED WITH FENTANYL CRI DURING OVARIOHYSTERECTOMY IN CATS

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Registration No.: 639

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**A thesis submitted in the partial fulfillment of the requirements for the degree of Master of Science in Surgery**

**Department of Medicine and Surgery**

**Faculty of Veterinary Medicine**

**Chattogram Veterinary and Animal Sciences University**

**Chattogram-4225, Bangladesh**

**June 2021**

# Authorization

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**Sabiha Zarin Tasnim Bristi**

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

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# DEDICATED TO MY SUPERVISORS AND FAMILY

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The Author

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## List of abbreviations and symbols

| Abbreviation | Elaboration |
|---|---|
| µg | Microgram |
| @ | At the rate of |
| % | Percentage |
| ℃ | Degree Celsius |
| ℉ | Degree Fahrenheit |
| < | Less than |
| > | Greater than |
| ASA | American Society of Anesthesia |
| BW | Body weight |
| CRI | Continuous rate infusion |
| CRT | Capillary refill time |
| CVASU | Chattogram Veterinary and Animal Sciences University |
| DAP | Diastolic arterial pressure |
| et al. | And his associates |
| et cetera | And the rest |
| $EtCO_2$ | End tidal $CO_2$ |
| HR | Heart rate |
| kg | Kilogram |
| L/min | Liter per minute |
| MAC | Minimum alveolar concentration |
| MAP | Mean arterial pressure |
| mg | Milligram |
| mL/min | Milliliter per minute |
| mm | Millimeter |
| MS | Master of Science |
| PIVA | Partial intravenous anesthesia |
| RR | Respiratory rate |
| SAP | Systolic arterial pressure |
| SAQTVH | Shahidul alam quadery teaching veterinary hospital |
| SDS | Simple descriptive scale |
| $SPO_2$ | Arterial hemoglobin saturation with oxygen |
| TIVA | Total intravenous anesthesia |

# Abstract

The study was conducted to estimate the comparison of maintenance anesthesia with propofol, and halothane combined with fentanyl CRI during ovariohysterectomy in cats admitted at Teaching Veterinary Hospital (TVH) in Chittagong Veterinary and Animal Sciences University (CVASU). Small animal anesthesia is difficult in the field condition while using proper analgesia. Propofol is a short-acting injectable anesthetic used to induce and maintain anesthesia. Halothane is the most extensively used inhaled anesthetic for general anesthesia, although it needs costly equipment and enormous amounts may cause environmental contamination. Both anesthetics lacks analgesic effect and needed multimodal approach combined with analgesic. This research investigated the anesthetic and cardiovascular effects of propofol or halothane anesthetic maintenance in cats receiving a fentanyl infusion during ovary hysterectomy, as well as the recovery from anesthesia. 18 cats were selected for ovariohysterectomy based on ASA I criteria. Propofol-fentanyl (PF) as total intravenous anesthesia (TIVA) and halothane-fentanyl (HF) as partial intravenous anesthesia (PIVA) were the two employed groups and each group had 9 cats. The cats were premedicated with xylazine hydrochloride (0.8 mg/kg), propofol (1 mg/kg, IV), and fentanyl (0.002 g/kg/h, IV) as constant-rate infusions (CRIs) in conjunction with either a CRI of propofol IV (TIVA) or halothane inhalation (PIVA). Propofol maintenance dosage was 10–11 mg/kg/hour, and end-tidal (FE'Halo) concentration of was 2-2.5 %. CRIs were started with 0.005 mg/kg fentanyl followed by 0.002 mg/kg/hour. Halothane-fentanyl was found to have lower mean arterial pressure (MAP) values at certain time intervals. While two patients in the HF group showed signs of restlessness, vocalizations, and paddling, recovery was uneventful in the PF group. Both procedures provided adequate anesthesia during surgery while having a negligible impact on cardiopulmonary function. However, the PF group takes longer than the HF group to recover from anesthesia.



***Keywords*:** Cardiopulmonary effects, Halothane, Propofol, Fentanyl, CRI, Cat

# Chapter-I: Introduction

There is a significant amount of history behind the practice of using canines and felines as study models. As a result of the widespread use of anesthetics in experimental animal medicine and the extensive variety of treatments that are carried out in clinical veterinary medicine, a large number of anesthetic regimens have been described. Each of these anesthetic regimens comes with its own individual set of benefits as well as limitations (Armitage-Chan, 2008).

The sterilization of cats is one of the surgical operations that is done in veterinary medicine more often than any other. In addition to concerns pertaining to welfare, members of the professional community cite concerns over population as a justification for this. It is feasible to reduce one's likelihood of acquiring reproductive disorders such as prostate cancer, testicular cancer, uterine cancer, ovarian cancer, and breast cancer. Another factor that must be taken into account is the undesirable behaviors that may be seen in stray populations. These behaviors, which can include vocalizing and roaming, can lead to feral and large colonies of animals (Howe, 2015).

A state of unconsciousness that is drug-induced, reversible, and under controlled conditions that cannot be aroused by painful stimuli is referred to as general anesthesia (Thurmon et al., 1996). General anesthesia can be broken down into three distinct stages: the induction phase, which involves bringing the patient from a conscious state to an unconscious one to make endotracheal intubation easier; the maintenance phase, which calls for a consistent surgical or diagnostic procedural depth along with appropriate muscle relaxation and analgesia without movement; and the recovery phase, which involves bringing the patient back to a conscious and aware state. Analgesia is one of the most important aspects of veterinary medicine since it plays a significant role in reducing or eliminating the patient's experience of pain and suffering. The vast majority of the time, a person has the intention of castrating or spaying an animal for their own good. This causes pain to an animal that wouldn't normally have to go through this kind of pain. It is suggested that canine and feline companion animals undergo an ovarian hysterectomy as a means of protecting themselves against a variety of reproductive issues and conditions. This method,

which is familiar to the majority of veterinary surgeons, has the potential to inflict moderate to severe pain (Hardie et al., 1997). It is essential to determine the proper medication of perioperative analgesia for each individual therapy in order to protect the well-being of the patient and prevent the development of long-term chronic pain syndromes (Woolf, 2011; Gurney, 2012).

For both induction and maintenance of anesthesia, injectable anesthetic medications are often employed, whereas maintenance of anesthesia is accomplished using inhaled agents (Clarke and Trim, 2013). Even while various agents give certain advantages, they lack other critical ideal attributes that are essential for the practice of contemporary anesthesia. There is not a single anesthetic agent that satisfies all of the requirements for an ideal anesthetic in the current practice of anesthesia. The intrinsic pharmacological effects of each anesthetic, the type of procedure and the length of time it will take, the availability of inhalation anesthetic equipment, the practitioner's level of expertise in the anesthetic technique, and other factors should be taken into consideration when selecting the most appropriate method for anesthetic maintenance. In addition, other considerations should also be taken into account. A multimodal approach is one that makes use of a variety of medications, each of which has a unique mode of action (Corletto, 2007). It is well known that a balanced analgesia may be obtained by mixing drugs in such a way that they each exert their impact on the nociception system of the body in a distinct manner (Brown et al., 2018). The concept behind the multimodal approach is to combine several distinct modes of operation while simultaneously reducing the quantity of each individual component. This is accomplished via the use of multimodal techniques. When it comes to the expense, this is a key concern, especially when seen from the perspective of emergency treatment. Because of this, there will be a reduced risk of experiencing adverse effects because of higher doses of the various drugs (Corletto, 2007).

Anesthesia that is based on a single anesthetic is not always the only choice available. Balanced anesthetic procedures are often an alternative. They involve the use of numerous medications in combination at the same time in order to accomplish the four key components of the optimal anesthetic state (amnesia, analgesia, muscular relaxation, and the stability of systems) with as few adverse effects as feasible (Tranquilli and Grimm, 2015). Cats are given inadequate analgesic in veterinary

clinical practice for a number of reasons (Benson et al., 1991; Hansen and Hardie, 1993). Many clinicians rely on visible indicators of pain such as vocalization, anxiousness, guarding of the affected body area, reluctance to move, and trembling. While these indicators of pain may be fairly reliable in dogs, cats behave in a different manner. Painful cats remain silent, hide, or assume a stiff and hunched posture, and this behavior may be overlooked. Opioids, such as morphine and oxymorphone, can result in central nervous system excitation and dysphoria in cats. As a result, some clinicians are reluctant to use potent opioids in this species. Nonsteroidal anti-inflammatory drugs used commonly in dogs are not well metabolized in cats, and can be toxic to the kidneys, liver, and gastrointestinal tract (Benson et al., 1991; Hansen and Hardie, 1993).

When compared to other species, cats need a much larger proportion of inhalation anesthetics. When anesthesia is maintained with just a single inhalation medicine, the risk for adverse effects (such as dose-related cardiovascular depression) is greater than when it is maintained with a mixture of sedatives or analgesics (Yasny and White, 2012; Steffey et al., 2015). In addition, the use of a single inhaled agent often requires the acquisition of expensive particular equipment and installations for the purpose of administration, and inhaled agents may contribute to the contamination of the atmosphere in the operating theater (Özelsel et al., 2019). An alternative to the use of a single drug for inhalation anesthesia is the combination of inhaled anesthetics with intravenous medicines (such as analgesics and/or sedatives). This technique, which is referred to as partial intravenous anesthesia (PIVA), improves cardiopulmonary parameters by lowering the amount of dose-related cardiovascular depressant effects caused by the inhaled anesthetic and reducing the amount of inhaled anesthetic that is required to prevent intraoperative awareness (Ilkiw et al., 1994; Muir III et al., 2003; Tranquilli and Grimm, 2015).

It is also possible to keep a patient under general anesthesia by administering total intravenous anesthesia (TIVA), which is an alternative to using inhaled anesthetics (Beths, 2017). Propofol has been shown to be the most successful medication for TIVA operations in dogs, cats, horses, calves, and goats (Beths, 2017). This is due to the pharmacokinetic properties of propofol, which allow for a fast start, ultra-short action, and rapid recovery from the effects of the drug. When compared to inhalation

anesthetic, the cost of injection anesthesia is lower, and it requires less specialized equipment for its administration and management (Beths, 2017).

Both propofol and halothane do not inhibit the reactions of the autonomic nervous system to noxious stimuli such as pain. Therefore, in order to induce general anesthesia, it is necessary to provide it in remarkably high dosages, and it must be paired with analgesic medications in order to achieve anesthesia during operations that are traumatic (Mendes and Selmi, 2003).

The simultaneous delivery of analgesics may minimize excessive anesthesia and protracted recovery durations, and although a2-agonists, non-steroidal anti-inflammatory medications or conduction blockage with local anesthetics can be utilized, the CRI of lipophilic opioid medicines, e.g., fentanyl, is especially ideal for this purpose. These medications lower the required induction dosage of propofol in canines and felines (Geel, 1991), and they have been used well as a single bolus or as CRIs to lower the minimum alveolar concentration (MAC) of volatile anesthetics in a variety of species (Murphy and Hug Jr, 1982; Hall et al., 1987; McEwan et al., 1993; Pascoe et al., 1994). It is probable that propofol will have the same effect of decreasing the required dosage. Greater hemodynamic stability and the use of lower total doses are two benefits that an opioid CRI has over repeated single injections. These advantages, in turn, allow for quicker recovery, generate less respiratory depression, and lessen the need for antagonists. In cats, a continuous rate infusion of alfentanil was tested and shown to maintain blood pressure while significantly lowering the minimum alveolar concentration (MAC) of isoflurane (Ilkiw et al., 1997; Pascoe et al., 1997). Cats were also able to sustain normotension when given a combination of CRI fentanyl and CRI propofol (Short and Bufalari, 1999; Mendes and Selmi, 2003). It is well recognized that the mixture of analgesic medications with various pharmacologic mechanisms will offer a better degree of analgesia than each drug provided alone. This may result in a significant reduction in the amount of hypnotic agents such as propofol and halothane that are required to achieve the same level of anesthesia (Steagall et al., 2006; Aguado et al., 2011). The hypothesis of this research was to judge anesthetic maintenance with propofol or halothane, while utilizing a fentanyl CRI as perioperative analgesia, may give equivalent outcomes with similar recovery quality.

The aim of the research was to compare halothane inhalation as partial intravenous anesthesia, propofol infusion as total intravenous anesthesia and both anesthetic with fentanyl CRI for maintaining anesthesia in cats. The comparison was based on the depth of anesthesia, cardiovascular, respiratory functions and recovery under anesthesia.

# Chapter-II: Review of literature

The selection of anesthetic agents is guided by a number of considerations, such as the need for analgesia during invasive procedures, the desire to have a few adverse effects as possible on the parameters under investigation, and the desire to keep the patient's physiological homeostasis stable. These considerations all contribute to a lower chance of unanticipated intraprocedural complications and mortality. Loss of consciousness and retrograde amnesia, analgesia (defined as an absence of the experience of painful stimuli), and muscular relaxation are the three components that make up the anesthetic trio. Because no single anesthetic has all of these qualities, the idea of balanced anesthesia can only be realized by the administration of many medications in conjunction with one another. There is now evidence that utilizing analgesic medications before and during general anesthetic helps the animal recover swiftly and painlessly, despite the idea that an animal is asleep during general anesthesia and so unable to experience pain (Hall, 1991).

One of the most crucial parts of veterinary medicine is analgesia, which is necessary to prevent pain and suffering. The majority of animals have neuter surgery, which is an elective treatment that causes discomfort to an otherwise pain-free animal. One such operation is ovarian hysterectomy, which is recommended for canines and felines in order to stop disorders and behaviors related to reproduction. The majority of veterinary surgeons are experienced with this treatment, which has the potential to cause moderate to severe discomfort (Hardie et al., 1997). By lowering the amount of peripheral and central sensitization, choosing the appropriate dose of perioperative analgesia for each specific treatment is essential to guaranteeing patient welfare and avoiding longer-lasting chronic pain syndromes (Woolf, 2011). Veterinarian surgeons must have access to the whole spectrum of analgesics in order to do this.

When referring to the procedure of sustaining anesthesia by the intravenous infusion of mixes of anesthetic drugs and analgesics, the term "total intravenous anesthesia" is the appropriate term to use (TIVA). In addition to the use of inhaled anesthetics, another method known as total intravenous anesthesia (TIVA) may be used to keep the patient under general anesthesia (Beths, 2017). Propofol has been shown to be the most acceptable agent for TIVA procedures in dogs, cats, horses, calves, and goats

(Bettschart-Wolfensberger et al., 2000; Beths, 2017). This is due to the fact that its pharmacokinetic features (which enable a quick onset), ultra-short action, and rapid recovery make it the most ideal candidate. The cost of injectable anesthetic is far cheaper than that of inhaled anesthetic, and it calls for significantly less specialized equipment for its administration and management. Halothane, like propofol, should be paired with analgesic medications for anesthesia during unpleasant operations; numerous pharmaceuticals have been used for this purpose in the past. Because it does not have any pain-relieving properties, halothane is comparable to propofol (Langley and Heel, 1988; Smith, 1994; Beths, 2017). Reduce the inspired concentration of inhalational anesthetic drugs by the use of a technique called partial intravenous anesthesia, which is also often referred to as drug infusion (PIVA). Procedures using partial intravenous anesthesia, often known as PIVA, have been used to treat patients suffering from neurological problems for a considerable amount of time. The PIVA or TIVA approach enables the use of very low quantities of volatile chemicals, or none of them at all, depending on which technique is being used. When it was found that PIVA and TIVA procedures may give better hemodynamic stability, comparable anesthetic management was applied to other regions, such as cardiac anesthesia. This was the case when it was discovered that PIVA and TIVA techniques (Liehmann et al., 2006; Wong and Morton, 2011). These methods are now being used in a wide variety of additional medical and veterinary contexts.

### 2.1 Preanesthetic

To prepare the patient for the placement of an intravascular catheter, premedication in the form of tranquilization or mild sedation is often given before intravenous induction, which is followed by maintenance by the inhalation or intravenous injection of different drugs (Clarke and Trim, 2013). The first stage of the anesthetic procedure for companion animals is the initial immobilization of the patient, which makes sure that the animal may be approached and handled without danger. This process aids in lowering patient stress and enhancing staff safety. It is then followed by the delivery of maintenance medicines as necessary (Clarke and Trim, 2013).

In veterinary medicine, sedatives are used for their anxiolytic characteristics and are often administered as pre-anesthetic treatment (Rankin, 2015). It is possible to

increase the quality of anesthesia induction and recovery, as well as the patient's overall welfare, by lowering the patient's level of fear and anxiety prior to the administration of anesthesia. It also makes it easier to handle patients and implant an IV catheter in them, which is extremely helpful when dealing with apprehensive and worried patients. In addition to this, the required dosage of the chemical used for induction and maintenance is lower. Sedative medicines, which normally do not exhibit significant analgesic effects on their own, are frequently coupled with an opioid analgesic for the treatment of pain. Because the opioid and sedative work together to provide a synergistic effect that enhances sedation, the sedative may be given at lower dosages without increasing the risk of experiencing unwanted effects (Rankin, 2015).

## 2.2 Induction

Propofol is a phenolic compound that induces CNS (Central Nervous System) depression and anesthesia by enhancing the GABAA receptor complex and increasing the neuroinhibitory effect of GABA (Concas et al., 1991). Propofol is used as an induction agent for general anesthesia. It is commonly administered IV as a bolus over 90 seconds and is usually given to effect (Sams et al., 2008). There is rapid uptake into the CNS which results in a rapid onset of action. It is also rapidly redistributed from the brain to other tissues and is metabolized by both hepatic and extrahepatic tissues resulting in a short duration of action of approximately 10 minutes. Propofol has minimal analgesic properties and must be paired with an analgesic for painful procedures. The most common effect on the cardiovascular system is transient arterial hypotension due to a decrease in systemic vascular resistance and peripheral vasodilation (Sams et al., 2008).

## 2.3 Maintenance

### 2.3.1 Total intravenous anesthesia

Total intravenous anesthesia also known as TIVA, is the process of inducing and maintaining general anesthesia with medications that are given solely through the intravenous (IV) route. This can be accomplished with the method of repeated bolus injection (RBI), or it can be accomplished with the technique of constant rate infusion. Both techniques are discussed further below (CRI) (Campbell et al., 2001).

Total intravenous anesthesia or TIVA is another name for this kind of anesthesia. Because of this, it is preferred for the drugs that are used in the process to have a short metabolic half-life and rapid clearance from the body. This will prevent the effects of the medication from piling up over time (Dundee and McMurray, 1984). The ideal anesthetic for healthy cats that have been brought in for elective procedures should have a rapid onset of action, a wide margin of safety, appropriate duration of action, anti-nociception, rapid and complete withdrawal so that the animals can be discharged immediately after the procedure in a state that is considered to be "home-fit." Additional ideal qualities are anti-nociception, an acceptable length of action, and a suitable duration of activity. Even though research into discovering anesthetic of this sort is still ongoing, there is not yet an anesthetic of this kind available currently. Propofol is a form of anesthetic medicine that is injected intravenously. It is a member of the alkyl phenol family and is also known as 2, 6-di-isopropylphenol (James and Glen, 1980). The usage of this hypnotic medication, which has a very brief duration of effect, has been given the go-ahead for use in both dogs and cats. It is a medicine that is administered intravenously that is used as an anesthetic and does not include any barbiturates. Additionally, it does not dissociate or accumulate in the body (Hall, Clarke, et al., 2001). Even when anesthesia is maintained with top-up doses or constant rate infusion (Adetunji et al., 2002; Ambros et al., 2008), it is still characterized by a smooth and speedy induction of anesthesia in dogs, the lack of an analgesic effect, dose-dependent cardiac depression, and short recovery periods. Propofol has practically none of the analgesic properties that are seen in other medications. Propofol must be used in conjunction with another analgesic drug, such as an opioid or an alpha-2 agonist, in order to effectively relieve discomfort before invasive procedures.

### 2.4 Propofol

Propofol is a generally noncumulative IV anesthetic drug that has a quick onset of action, an ultrashort duration, and is not barbiturate. Produces dose-dependent depression of the cerebral cortex and CNS polysynaptic reflexes; enhances the effects of nondepolarizing neuromuscular blocking drugs; produces sedation-hypnosis similar to that produced by other hypnotics; binds to GABA A receptors; acts as a sodium channel blocker (Tranquilli et al., 2013).

### 2.4.1 Effects on different organs and systems

#### 2.4.1.1 Central nervous system

Propofol administered intravenously causes a fast depression of the central nervous system (CNS) as well as the induction of anesthesia. In patients with normal intracranial pressure, there is a minor reduction in cerebral perfusion pressure; however, in patients with a raised intracranial pressure, there is a large decrease in cerebral perfusion pressure, which may not be advantageous (Herregods et al., 1988). During the administration of propofol, brain reactivity to carbon dioxide and cerebral metabolic autoregulation are preserved (Artru et al., 1992). However, this response may be altered by the concurrent administration of other medicines such as opioids. Propofol causes alterations in the cortical EEG that are comparable to those caused by barbiturates. These changes include the occurrence of burst suppression when large dosages of the drug are administered (Artru et al., 1992). Propofol is an anticonvulsant that may be used in the treatment of seizures that are resistant to other types of medication (Cheng et al., 1996; Steffen and Grasmueck, 2000).

#### 2.4.1.2 Cardiovascular system

A reduction in arterial blood pressure is the most notable cardiovascular impact that may be brought about by the administration of propofol. There is also an observed lessening in the systemic vascular resistance as well as the cardiac output (Brüssel et al., 1989; Goodchild and Serrao, 1989). It would suggest that the dosage (as well as the plasma concentration) has a role in the myocardial depression and vasodilation (Goodchild and Serrao, 1989). Patients who are hypovolemic (Ilkiw et al., 1991), elderly, or who have reduced left ventricular function (Pagel et al., 1998) are more likely to experience the more severe manifestations of these cardiovascular consequences. The administration of propofol, on the other hand, does not often result in a compensatory rise in heart rate as thiopental administration does. It would seem that propofol may make the myocardium more susceptible to epinephrine-induced arrhythmias; nonetheless, it does not appear to be arrhythmogenic.

#### 2.4.1.3 Respiratory system

Propofol, much like thiopental, is known to elicit a dose-dependent decrease of breathing as well as postinduction apnea, which is often accompanied by temporary cyanosis (Muir and Gadawski, 1998). The occurrence of apnea is linked to the dosage as well as the rate of administration, with apnea being more likely to occur when fast injection rates are used (Muir and Gadawski, 1998). Propofol decreases the ventilatory response to hypoxia (Blouin et al., 1993) and carbon dioxide (Goodman et al., 1987), and the introduction of opioids may increase the impact that propofol has on ventilation (Taylor et al., 1986). When propofol is delivered at a constant rate infusion, respiratory effects are also noted, with propofol lowering the tidal volume and respiratory rate (Goodman et al., 1987).

#### 2.4.1.4 Hepatic, renal, and gastrointestinal systems

Propofol does not have any negative effects on the blood flow in the liver or the glomerular filtration rate in dogs (Haberer et al., 1993). Propofol has been demonstrated to be a remarkably effective antiemetic when administered to humans. In point of fact, subanesthetic dosages of propofol may be administered after anesthesia in order to cure nausea and vomiting (Apfel et al., 2005). However, this effect has not been proven in domestic animals.

#### 2.4.1.5 Muscles

Propofol, much like thiopental, has a relaxing effect on the muscles. Myoclonic movements, on the other hand, have been documented on occasion in both people and canines (Smedile et al., 1996; Nimmaanrat, 2005). These motions come to a natural conclusion on their own.

#### 2.4.1.6 Fetal/neonatal effects

Propofol is able to easily pass through the placenta, although it is quickly eliminated from the blood of the neonate (Andaluz et al., 2003). It is an option that is appropriate for dogs that will be having cesarean section due to the fact that its effects on healthy pups are limited (Doebeli et al., 2013).

#### 2.4.1.7 Efficacy in relieving pain

Neither antinociception nor hyperalgesia is produced by propofol in the body. As a result, animals who are going to be having painful treatments have to be given the proper analgesics as part of the anesthetic strategy (Tranquilli et al., 2013).

When given on a regular basis, repeated doses of propofol have the potential to cause oxidative damage to feline red blood cells (Andress et al., 1995). One research found that cats who were given propofol for many days in a row had Heinz body formation, facial edema, widespread malaise, anorexia, and diarrhea. Propofol treatment resulted in a considerable rise in the production of Heinz bodies by the third day, and recovery durations were considerably lengthened when the drug was given for a second consecutive day (Andress et al., 1995). On the other hand, recurrent propofol anesthesia was investigated in a different investigation, and it was found that no significant hematologic alterations were identified (Bley et al., 2007). Although there has been concern regarding this formulation due to the potential adverse effects of benzyl alcohol on feline blood and nervous systems, it has been shown that administration to healthy cats of normal to high clinical doses of the formulation did not cause organ toxicity (Taylor et al., 2012). Although there has been concern regarding this formulation due to the potential adverse effects of benzyl alcohol on feline blood and nervous systems, it has been shown that this formulation does not cause organ Additionally, the lipid-free microemulsion formulation was tested on cats (Cleale et al., 2009; Wiese et al., 2010), and when compared to the lipid emulsion formulation, it produced responses in pharmacokinetics, pharmacodynamics, and physiology that were equivalent (Cleale et al., 2009).

### 2.5 Partial intravenous anesthesia

It is possible to lower the inspired concentration of inhalational anesthetic agents by administering medicines via an intravenous infusion, which is referred to as partial intravenous anesthesia (PIVA). It is possible that the use of PIVA procedures in conjunction with inhalational anesthesia may seem to be more troublesome and expensive than it will be worth, and this may be the case for regular, brief elective surgery (Ko and Berman, 2010). The use of PIVA to help in the maintenance of anesthesia is, nevertheless, useful, and the approach has gained popularity in the field of specialized veterinary anesthesia for certain operations, as well as in critically sick

patients and/or for pain. The phrase anesthetic-sparing effect of PIVA medicines is chosen in the clinical context over the term lowering of minimum alveolar concentration (MAC), which is determined under controlled laboratory circumstances. The following are some of the many benefits of using PIVA: i) A high and consistent level of anesthetic quality is achieved through the use of PIVA methods, which maintain plasma concentration. The infusion may be stopped after the anesthesia or surgical time is complete, or it can be extended throughout the recovery phase until it is determined that it is no longer required. ii) Improved support for the hemodynamic system. When they are given at clinical infusion rates, several of the medications that are used for PIVA have little of a detrimental influence on the patient's hemodynamic stability. These hemodynamically stable infusions have the potential to also have a great capacity to save volatile anesthetics. Ilkiw et al. (1994) found a considerable improvement in cardiovascular function when a fentanyl infusion was used and the concentration of enflurane was reduced by about 65 percent. This was due to the anesthetic-sparing ability of the infusions, which can allow for a reduction in the inspired concentration of the volatile agent. This, in turn, reduces the negative effects of the volatile agent on hemodynamic stability. They issued a warning that anticholinergic medication could be necessary in order to restore the severe bradycardia that was produced by fentanyl (Ilkiw et al., 1994). However, the potential to alleviate respiratory depression may not be as evident since injectable medications can have their own effects on respiratory function, which might be increased using volatile agents at the same time. As a result, it is possible that ventilatory assistance will still be necessary. The recovery process may be less difficult, and many medications may be used throughout the postoperative period without any problems. Many of the medications act as sedatives, and when combined with analgesics, they may provide for a smoother and more manageable transition from the effects of general anesthesia into the stages of recovery and consciousness. It is possible to make incremental reductions in the patient's infusion rates, which will enable the patient to make a full recovery in an under-control way. It is still necessary to keep a careful eye on the patient when they are in the postoperative period. This is done to prevent the patient from being too sedated and maybe losing their airway reflexes. iv) The majority of PIVA procedures include analgesia in addition to sedation for the patient.

### 2.5.1 Inhalation anesthesia

Inhalation anesthetic agents are a collection of gases and volatile liquids that induce general anesthesia. When referring to anesthesia, the term "inhalation" refers to the act of breathing in gases or vapors together with oxygen. In the field of veterinary medicine that deals with companion animals, inhalant anesthetics are often utilized. They are regarded as preferable to injectable drugs because to their quick induction, rapid recovery, and improved control over the intensity and duration of anesthesia, in addition to more acceptable physiologic responses (Sedgwick, 1986). Despite the growing demand for general anesthesia, there has not been a significant reduction in the overall canine anesthetic death rate during the last two decades (Dyson et al., 1998; Brodbelt et al., 2008; Bille et al., 2012).

A specialized device is used to deliver the inhaled drugs to the patients. This device is equipped with a supply of oxygen ($O_2$) as well as a breathing circuit for the patient, which may consist of an endotracheal tube or a face mask, and it also ensures the correct removal of carbon dioxide ($CO_2$). Because they all increase arterial oxygenation and make lung breathing easier, all these pieces of equipment contribute to a reduction in the risk of morbidity and death among patients (Steffey and Mama, 2007). All animals have a dose-related decrease in their cardiopulmonary function after receiving inhalation anesthesia (Polis et al., 2001). Anesthetics that include halogens, such as halothane and isoflurane, have the potential to alter both the pace and rhythm of the heart. In the field of veterinary medicine, halothane and isoflurane have both been found used in clinical practice (Mutoh et al., 1997).

### 2.5.2 Halothane

Many therapeutic procedures continue to see value in using halothane as an anesthetic, despite the fact that its usage dates back many decades. In the field of inhalant anesthesia, it was a significant step forward when it was first introduced. The year 1956 was the year when halothane, which has the chemical structure of 2-bromo-2-chloro-1,1,1-trifluoroethane, was first introduced into the field of medical and veterinary anesthesia (Hall, 1957). After its invention for use as an anesthetic in humans by Sweking in 1951, halothane was initially utilized in veterinary anesthesia for the first time in 1956 (Suckling, 1957). It was so much more effective than any of the other agents that were already in use across the globe. Prior to the discovery of the

potentially lethal consequences that were connected with halothane usage in human anesthesia, the substance was widely employed. Guinea pigs are especially vulnerable to the effects of anesthesia (Lunam et al., 1985). The use of halothane as an inhalation agent was the first to be successful in the treatment of both big and small animals. Although halothane is not considered to be "approved" for use in human or animal medicine in North America or Europe, it is nevertheless used in other regions of the globe and continues to be included on the list of essential medicines maintained by the World Health Organization (WHO, 2019).

Halothane is a colorless liquid that may be kept in dark bottles with thymol as a preservative since it does not volatilize as much as halothane. Because thymol causes a sticky residue to build within calibrated vaporizers, anesthetic production is reduced, and the vaporizers need to be cleaned out during periodic maintenance (Hall and Clarke, 2014). It has a distinct odor that is reminiscent of chloroform, and it tastes sweet and acrid. The solubility of halothane in water is limited, although it may be dissolved in alcohol. The specific gravity of halothane ranges between 1.872 and 1.877 at 20 degrees Celsius, and its vapor pressure is 243 millimeters of mercury.

In terms of its chemical composition, halothane is categorized as a halogenated hydrocarbon; nevertheless, in terms of its chemical composition, it is not connected to the ethers (West et al., 2014). A non-explosive and moderately stable anesthetic with a low blood-gas solubility coefficient, halothane has the following properties: 2.54. Low gas solubility in comparison to ether, which was the most commonly used inhalant anesthetic agent before halothane, which indicates that it enables a smooth and rapid induction of anesthesia as well as recovery from it. Additionally, the incidence of postoperative nausea and vomiting is low, and it is relatively less toxic than inhalant anesthetic agents that were previously used. Because it does not react with soda lime, halothane may be used in systems that are closed loops. The advantages of halothane include its cheap cost, relative safety, potency, and controllability, as well as its inflammability. The following are the values that have been published for the Minimal Alveolar Concentration (MAC; percent) in oxygen for halothane in different species: Dog = 0.76; Cat = 0.82-1.22; Horse = 0.88; Human = 0.76.

### 2.5.3 Effects on different organs and systems

#### 2.5.3.1 Nervous and musculoskeletal systems

The central nervous system is depressed to a dose-dependent degree by halothane, while analgesics bring about an increase in cerebral blood flow. Because moderate muscular relaxation during light anesthesia is a poor analgesic and does not add to postoperative analgesia, preemptive analgesic supplementation is particularly helpful in reducing the need for postoperative pain medication (Hall and Clarke, 2014). A hereditary muscle deficiency may be activated in susceptible individuals, pigs, dogs, and cats, which results in malignant hyperthermia. It causes the condition (Muir and Hubbell, 2014).

#### 2.5.3.2 Respiratory system

A dose-related respiratory depression is produced by halothane, which leads to a gradual rise in $PaCO_2$ concentration. Animals have a tendency, when under the influence of halothane anesthesia, to breathe on their own more effectively than when they are under the influence of more recent medicines (Steffey, 2002). Because, unlike isoflurane, it does not irritate the mucosa of the respiratory tract, it is possible to induce anesthesia with it without the patient having to hold their breath (Hall and Clarke, 2014).

#### 2.5.3.3 Cardiovascular system

At therapeutic concentrations, the negative inotropic action of halothane results in bradycardia and a drop in arterial blood pressure in all mammalian species. Halothane also produces a small amount of transmission blockage in sympathetic ganglia, although this has minimal impact on the cardiovascular system. The vagus nerve is responsible for the majority of cases of bradycardia (Muir and Hubbell, 2014). It may produce hypotension that is connected to the depth of anesthesia, as well as a reduction in myocardial contractile function at low concentrations and vasodilation at high concentrations when it is present in large enough quantities (Muir and Hubbell, 2014). The heart becomes more susceptible to tachyarrhythmias caused by catecholamines after exposure to halothane. $CO_2$ buildup, low oxygen levels, and the release of catecholamines are all linked to arrhythmias in the heart (Dunlop et al., 1987; Steffey and Mama, 2007). Due to increased systemic vascular resistance at the start of surgery blood pressure tends to increase (Wagner et al., 1995).

#### 2.5.3.4 Reproductive system

It has been shown that halothane may pass the placental barrier and cause teratogenic consequences. These anesthetics provide a possible threat to the unborn puppies and kittens of pregnant dogs and cats (Muir and Hubbell, 2014).

#### 2.5.3.5 Absorption, fate, and excretion

The microsomes in the liver are responsible for the metabolism of halothane, which results in the production of trifluoroacetic acid, bromide, and chloride radicals, which are then eliminated in the urine over a period of time ranging from hours to days (Muir and Hubbell, 2014).

#### 2.5.3.6 Precautions

Patients who have malignant hyperthermia, impaired hepatic function, cardiac arrhythmias, increased CSF or head injury, myasthenia gravis, or pheochromocytoma should not be given halothane since it is not safe for them to take (cardiac arrhythmias due to catecholamines) (Muir and Hubbell, 2014).

### 2.6 Perioperative analgesia

The preoperative, intraoperative, and postoperative periods all make up what is known as the perioperative period (Gurney, 2012). At first, it was believed that administering "pre-emptive" analgesics before the incision would minimize nociceptive processing, so preventing intraoperative amplification of pain pathways and, as a result, minimizing the amount of postoperative pain experienced by the patient. It is now generally understood that variables present throughout any period of the peri-operative process might contribute to the onset and intensity of postoperative pain. These include genetic susceptibility, noxious inputs before surgery, tissue damage and inflammation during surgery, and inflammatory reactions after surgery (Katz et al., 2011). It has been shown via research on humans that the administration of analgesia during the perioperative period, also known as preventative analgesia, is superior to the administration of pre-emptive analgesia on its own. It is generally agreed that preventative analgesia is the best strategy for inhibiting the transmission of primary afferent nociceptive signals to the spinal cord and, as a result, avoiding the sensitization of both peripheral and central pain pathways as well as the amplification of pain pathways (Vadivelu et al., 2014). Even though there have only been a few

numbers of research conducted on animals comparing pre-emptive and preventative analgesia, the findings of studies conducted on humans may almost certainly be generalized. The incisional noxious input kicks off these processes, which are then enhanced by additional inflammatory inputs that persist throughout the post-operative period. In order for analgesics to be effective at the moment of noxious stimulation, it is essential that they be administered with enough time in between doses to allow for optimal bioavailability. In addition, it is essential that their effects continue into the post-operative period, which is a time when patients frequently experience additional inflammatory or sensory input (Kissin and Weiskopf, 2000), and that additional analgesia be given during the perioperative period when it is clinically necessary to do so.

### 2.7 Use of opioids in veterinary practice

The administration of opioids and multimodal analgesia has increased within the veterinary profession over the last 20 years (Hunt et al., 2015). This is a result of a greater range of licensed analgesics available, an increasing understanding of how to treat different forms of pain, an improvement in pain assessment techniques and a shift in client expectation (Hunt et al., 2015).

Opioids are an excellent choice both for use during surgery to alleviate pain and as a supplement to inhalational anesthetic and injectable anesthetics. Opioids are often given as part of combination premedication, and the duration of their action may be extended by administering additional of the drug during the surgical procedure. During anesthesia, opioids may also be given as an intravenous infusion into the patient's vein. Anesthetic sparing may occur with opioids that have a high intrinsic activity at the mu-opioid receptor, particularly in dogs. In dogs, mu-opioid agonists can reduce the concentration of volatile agent needed to maintain a surgical plane of anesthesia by as much as 50-60% (Steffey et al., 1994; Hellyer et al., 2001; Muir et al., 2003). There is a maximum limit to the quantity of anesthetic that can be saved while using opioids, and increasing the dosage does not result in a further reduction in the amount of volatile agent that is needed (Murphy and Hug Jr, 1982; Ilkiw et al., 2003). When using the same mu-opioid agonists in cats, the anesthetic sparing effect is less noticeable, although a decrease of 15-20% in the amount of volatile anesthetic required is noted (Ilkiw et al., 2002). There is a possibility that the anesthetic sparing

effect is connected to the capacity of mu-opioid agonists to stimulate the central nervous system in some people rather than causing depression in those persons. Stimulation of the central nervous system is more likely to occur in cats when greater doses, like those used in dogs, are administered. In the field of veterinary anesthesia, the opioids morphine, hydromorphone, fentanyl, sufentanil, and remifentanil are the ones that are often administered by infusion the most frequently (Hall et al., 1987; Hellebrekers and Sap, 1991; Michelsen et al., 1996; Ilkiw, 1999; Ilkiw et al., 2002; Muir III et al., 2003; KuKanich et al., 2008; Ferreira et al., 2009). It is possible that anticholinergics will be necessary in order to address bradycardia brought on by a mu-opioid-induced increase in vagal tone; nonetheless, mu-opioid agonist infusions generally produce adequate hemodynamic stability. Mu-opioid agonists, on the other hand, have been shown to have a respiratory depressive effect, which means that supplemental ventilation may be necessary (Liehmann et al., 2006).

### 2.7.1 Fentanyl

Fentanyl is a highly lipid soluble, short-acting synthetic μ opioid agonist. A single dose of fentanyl administered intravenously has a more rapid onset and a much briefer action than morphine. Peak analgesic effects occur in about 5 min and last approximately 30 min (Gutstein, 2001; Stoelting and Hillier, 2012). Rapid redistribution of the drug to inactive tissue sites, such as fat and skeletal muscle, leads to a decrease in plasma concentration and is responsible for the prompt termination of clinical effects. In most veterinary species, the elimination half-life after a single bolus or a brief infusion is in the range of 2 to 3 h (Carroll et al., 1999; Lee et al., 2000; Maxwell et al., 2003). Administration of large doses or prolonged infusions may cause saturation of inactive tissues, with termination of clinical effects becoming dependent on hepatic metabolism and renal excretion (Gutstein, 2001; Stoelting and Hillier, 2012). Thus, the context-sensitive half-life of fentanyl increases significantly with the duration of the infusion, and clinical effects may persist for an extended period following the termination of a long-term intravenous infusion.

Side effects associated with fentanyl administration are similar to those of the other full μ-agonist opioids. In general, cardiovascular stability is excellent with fentanyl, and intravenous administration is not associated with histamine release (Gutstein, 2001; Stoelting and Hillier, 2012). Bradycardia may be significant with bolus doses,

but readily responds to anticholinergics if treatment is warranted (Branson et al., 2001; Gutstein, 2001). In human patients, muscle rigidity, especially of the chest wall, has been noted after administration of fentanyl or one of its congeners (Andrew Bowdle, 1998; Fahnenstich et al., 2000; Müller and Vogtmann, 2000). The potential significance of this adverse effect in animal patients is not clear at this time, and the risk is considered minimal if large, rapid bolus administrations are avoided. Clinically, fentanyl is used most frequently in dogs and cats, but is also a potentially useful analgesic in other species, including horses, cows, sheep, goats, and pigs. Because of its shorter action, fentanyl is typically administered as a continuous infusion to provide analgesia. Intravenous fentanyl can be infused at relatively low doses to supplement analgesia intraoperatively and/or postoperatively in dogs and cats. It is also useful for management of nonsurgical pain, such as that associated with pancreatitis. Alternatively, larger doses can be administered, often in combination with a benzodiazepine like midazolam, to induce general anesthesia in canine patients with cardiovascular or hemodynamic instability. Similarly, higher infusion rates of fentanyl can be used as the primary anesthetic agent for surgical maintenance in patients who will not tolerate significant concentrations of volatile inhalant anesthetics (Hellyer et al., 2001; Martín et al., 2001; Mendes and Selmi, 2003). In the clinical setting, there are few reports of intravenous fentanyl administration in large animal species, though fentanyl infusions have been employed in a variety of surgical animal research models involving calves, sheep, and pigs (Wilson et al., 2000; Kurita et al., 2003). In addition to intravenous administration, fentanyl may be deposited into the epidural space to produce analgesia. Because of its high lipid solubility, epidural fentanyl, unlike morphine, is rapidly absorbed into the systemic circulation. Consequently, the clinical effects associated with a single bolus of epidural fentanyl resemble those of an intravenous injection. However, the benefits of neuraxial administration can be achieved by administering epidural fentanyl as a continuous infusion through an indwelling epidural catheter, often in combination with other analgesic agents. This technique is typically used in canine patients for management of severe acute pain, but it may have additional applications for the management of chronic pain as well. The development of novel, less invasive, routes of opioid administration for use in human patients led to the marketing of transdermal fentanyl patches (Duragesic). The patches are designed to release a constant amount of fentanyl per hour that is then absorbed across the skin and taken up systemically.

Fentanyl patches are designed for human skin and human body temperature, but their use has been evaluated in a number of veterinary species (Egger et al., 1998, 2003; Carroll et al., 1999; Robinson et al., 1999; Franks et al., 2000; Wilkinson et al., 2001; Gellasch et al., 2002; Gilberto et al., 2003; Maxwell et al., 2003). Though transdermal fentanyl appears to be an effective means of providing analgesia in a number of clinical settings, substantial variations in plasma drug concentrations have been documented, and significant lag times after patch placement are common prior to onset of analgesia (Egger et al., 1998, 2003; Carroll et al., 1999; Lee et al., 2000). Furthermore, changes in body temperature have been shown to affect fentanyl absorption significantly in anesthetized cats (Pettifer and Hosgood, 2003), and it is likely that other factors associated with skin preparation and patch placement have the potential to alter plasma fentanyl levels and analgesic efficacy substantially. Two recent studies evaluating the efficacy of pluronic lecithin organogel (PLO gel) delivery of fentanyl through skin in dogs and cats concluded that this method of administration did not result in measurable plasma concentrations and thus could not be justified as an effective means of systemic administration (Krotscheck et al., 2004; Robertson et al., 2005).

Recovery Pain can have severe detrimental effects within the postoperative period. Effects include delayed or poor wound healing, increased incidence of infection or sepsis, increased incidence of tumor metastasis, cardiovascular stress or compromise, increased metabolism with a negative energy balance, increased tissue catabolism, and a prolonged convalescence. Recovery Pain can have severe detrimental effects within the postoperative period. Effects include delayed or poor wound healing, increased incidence of infection or sepsis, increased incidence of tumor metastasis, cardiovascular stress or compromise, increased metabolism with a negative energy balance, increased tissue catabolism, and a prolonged convalescence. Pain is believed to be the cause of the rough recovery, rapid acting opioid analgesics (e.g., fentanyl) will reduce this adverse effect (Tranquilli et al., 2013).

There are few reports on the use of propofol in cats, generally for induction rather than maintenance. The use of propofol and halothane with fentanyl CRI in felids for maintenance of anesthesia in individual cases has been documented. However, it has been suggested the infusions of propofol (0.05-0.2 mg/kg/minute) may lead to

prolonged recovery when used for longer than 20 minutes of maintenance in cheetahs (Woc Colburn et al., 2009). To be effective and practical, an anesthetic agent should allow for flexible control of anesthetic depth to achieve a desired level of anesthesia and to maintain stable cardiopulmonary function at effective doses. A well-equipped operation theater can provide all the anesthetic facilities to patient in PIVA techniques there the anesthetic should also be practical to administer in a field setting in TIVA technique while analgesia is well maintained in both techniques. As a result, there is currently few literature detailing strategies for anesthetic maintenance with fentanyl CRI and none comparing the effects either propofol to halothane in cats.

# Chapter-III: Materials and Methods

## 3.1 Study period

This research was conducted at the Shahidul Alam Quadery Teaching Veterinary Hospital (SAQTVH), Chattogram Veterinary and Animal Sciences University (CVASU), in Chattogram, Bangladesh. From January 2021 to December 2021.

## 3.2 Study design

This experiment included a total of eighteen (n=18) local female cats weighing between 3kg to 4 kg and ranging in age from 6 to 16 months. On each patient, a preoperative anamnesis and a pre-anesthetic physical examination were done. For this investigation, all samples were randomly divided into two groups (n = 9 in each group; Group PF & Group HF). All cats were classified as American Society of Anesthesiologists (ASA) Grade 1 (appendix 1) based on a physical assessment (normal healthy patient). Before anesthesia, food and drink were withheld for 12 hours. Prior to premedication, the cat's body mass (BW), heart rate (HR), respiration rate (RR), and rectal temperature were measured.

## 3.3 Preanesthetic procedures

Before induction of anesthesia, xylazine HCl @ 0.8 mg/kg was administered intramuscularly (IM) for sedation (Dzikiti et al., 2007). After 10 minutes, the patients' levels of drowsiness were evaluated using a 0-3 scale, with 0 indicating no sedation, 1 indicating light sedation (moderate restraint necessary), and 2 indicating moderate sedation (mild restraint required), and 3 indicating profound sedation (No Resistance).

## 3.4 Anesthesia Protocol

Animals were moved from the preparation area to the main theater ten minutes after sedative scoring. Once all cats were sedated, a 22-gauge catheter was inserted into the left cephalic vein, and an infusion pump was used to provide 0.9 percent sodium chloride solution at a flow rate of 10 mL/kg/hr. Propofol @ 1 mg/kg was injected slowly until endotracheal intubation could be performed in order to produce general anesthesia. The larynx was desensitized with one dose of a 10% lidocaine aerosol prior to tracheal intubation.

After endotracheal intubation, all cats were connected to a non-re-breathing system with an oxygen flow rate of 200 mL/kg/min and CRIs were initiated with a loading dose of fentanyl @0.005mg/kg followed by 0.002mg/kg/hour.

**Figure 1: Desensitization of larynx with 10% lidocaine spray**

**Figure 2: Endotracheal intubation in Cat.**

### 3.5 Maintenance of anesthesia

Propofol-fentanyl group: Initial CRIs of propofol at 10 mg/kg/hour. The propofol infusion rate was adjusted to maintain surgical anesthesia. Propofol infusion started

immediately after completing the administration of the last bolus of propofol for induction of general anesthesia.

Halothane-fentanyl group: Anesthesia was maintained with halothane vaporizer for induction (3.5% to 4%) and the vaporizer setting was adjusted from 1.5% to 2.5% according to the depth of anesthesia. The administration rate was adjusted to maintain surgical anesthesia.

Propofol was given out via a device called an infusion pump for the purpose of anesthetic maintenance (InfusoVet Easy II, Eickmeyer, Germany). Following the successful completion of the injection of the last bolus of propofol for the induction of general anesthesia, the propofol infusion was started immediately. Using an infusion pump device, simultaneous administration of IV fluids, propofol infusions, and fentanyl infusions were carried out.

### 3.6 Cardiopulmonary Variables Measurement

The patient was monitored using a standard anesthetic log sheet (appendix 3). Noninvasive systolic (SAP), diastolic (DAP), and mean arterial (MAP) blood pressures, heart rate (HR), oxygen saturation of the hemoglobin (SpO2), respiratory rate (RR), end-tidal CO2 (Et-CO2), rectal temperature was monitored with veterinary patient monitoring system (LifeVet M, SN:260647-M17A08890009, Eickmeyer, Germany). Eye position (straight, down), jaw tone, pedal reflex, and capillary refill time (CRT) were all measured to identify the level of anesthesia.

Heart rate (HR), mean arterial pressure (MAP), respiratory rate (RR), and core body temperature were monitored continuously throughout induction and maintenance of anesthesia at 5-minute intervals.

An electric thermometer probe was inserted into the rectal mucosa to get rectal temperature readings. Electrodes were attached to the skin of the patient's right and left elbows, patella to record heart rate and rhythm. Oscillometry was used to determine the systolic and diastolic arterial blood pressures. The cuff was applied to the patient's left antebrachium. The cat's $SpO_2$ was measured using a pulse oximeter (by placing the infrared sensor probe on its tongue). A heating pad was used to

regulate body temperature. The cats were extubated after they regained consciousness from anesthesia and developed a swallowing reflex.

**Figure 3: Maintenance of anesthesia during the surgical procedure.**

### 3.8 Evaluation of Anesthetic Depth

All cats had an ovariohysterectomy done by the same surgeon. To ensure that both groups received an acceptable and equivalent degree of anesthesia same anesthesiologist always made minute-to-minute adjustments to the rate of delivery of propofol-fentanyl (in TIVA) or halothane-fentanyl (in PIVA) to maintain surgical anesthesia, based on the patient's clinical signs of absence of palpebral reflex, ventro-medial eye rotation, loss of mandibular and neck muscle tone, absence of purposeful movement in response to surgical stimulation and increases or decrease in HR and MAP of  20% from baseline levels indicate a mild autonomic response.

The following actions were followed if the anesthetic depth was deemed insufficient when a significant palpebral or withdrawal response, central rotation of the eyeball, or heart rate or blood pressure rose by 20% from baseline values (measured before skin incision) happened at any point during anesthesia: Halothane concentration was raised by 0.5 percent in group HF (PIVA), while 1 mg/kg of propofol was administered in group PF (TIVA).

At the following periods, average values for HR, RR, systolic, diastolic, and mean blood pressure, temperature and EtCO2 were recorded: T0: before skin incision; baseline measures were averaged over 5 minutes; T1: during skin incision; T2: during excision of the left ovary; T3: during excision of the right ovary; T4: during excision of the uterus; T5: during maintenance when surgery had commenced but when intense surgical stimulation was not present; and T6: at skin closure. Data gathered at T1, T2,

T3, T4, and T5 were the average of measurements taken during the time period, with the exception of T0, which was a single time point.

Surgery time, anesthetic time, and time to extubation were all documented from the moment the first incision was made until the final stitch was placed.

Quality of anesthesia were evaluated using 1-3 scale with 1 Very responsive to surgical stimulation (gross purposeful movement, such as lifting head, chewing, and vocalization), 2 Mild response to surgical stimulation, and 3 No response to surgical stimulation.

Pain assessment was done with the simple descriptive scale (appendix 4), as in veterinary medicine, animals cannot self-report pain, thus a veterinarian observes their behavior to determine pain intensity. No pain, mild pain, moderate pain, severe pain is used to characterize pain intensity on the SDS. Each expression's number becomes the pain score.

### 3.9 Recovery

At the moment of extubation, which was determined by the restoration of the swallowing reflex, cats were unplugged from the inhalation anesthetic supply circuit. The time it took to do the initial head lift and the time it took to achieve a sternal position (the amount of time that passed between when the vaporizer or infuser pump was turned off and when the sternal posture was achieved) were both recorded.

**Table 1. Simple descriptive scale (SDS) used to measure the quality of recovery (Hunt et al., 2013)**

| SDS | Quality of Recovery |
|---|---|
| 0 | Poor – animal shows major signs of excitement during recovery such as thrashing or moving around rapidly unaware of surroundings, which do not respond to gentle handling. |
| 1 | Moderate – animal shows some signs of excitement during recovery such as thrashing or moving around rapidly unaware of surroundings, which resolve with gentle handling. |
| 2 | Good – mild signs of excitement, which resolve quickly so that the animal becomes calm |
| 3 | Excellent – animal is calm and relaxed during recovery |

### 3.10 Statistical analysis

Data was 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+ SD and 't' test was used to compare the means at different time intervals among the two groups. ANOVA was done to compare the mean value of different physiological parameters during the anesthetic process among the surgical events. $P < 0.05$ values were considered significant.

# Chapter-IV: Results

## 4.1 Preanesthetic Sedation and Induction Dose of Propofol

The administration of xylazine moderately sedated all cats. The median score recorded for both the PIVA and TIVA regimens was 2. For all procedures, the average doses of propofol needed for induction of anesthesia were 1mg/kg.

## 4.2 Cardiopulmonary Variables

The cardiopulmonary parameters of the cats in each anesthesia group were measured every 5 minutes from the time of induction of anesthesia (0 min) to 60 minutes during operation.

### 4.2.1 Findings of the heart rate (HR)

All data were analyzed using the mean standard deviation statistic. A significant increase in heart rate was observed in the HF and PF group when compared to the value that was taken as the baseline immediately after the circuit was attached to the patients (Figure 4). At 30, 35 and 50 minutes after receiving anesthesia, there was a statistically significant difference ($p<0.01$) in the participants' heart rates between the two groups (Figure 4).

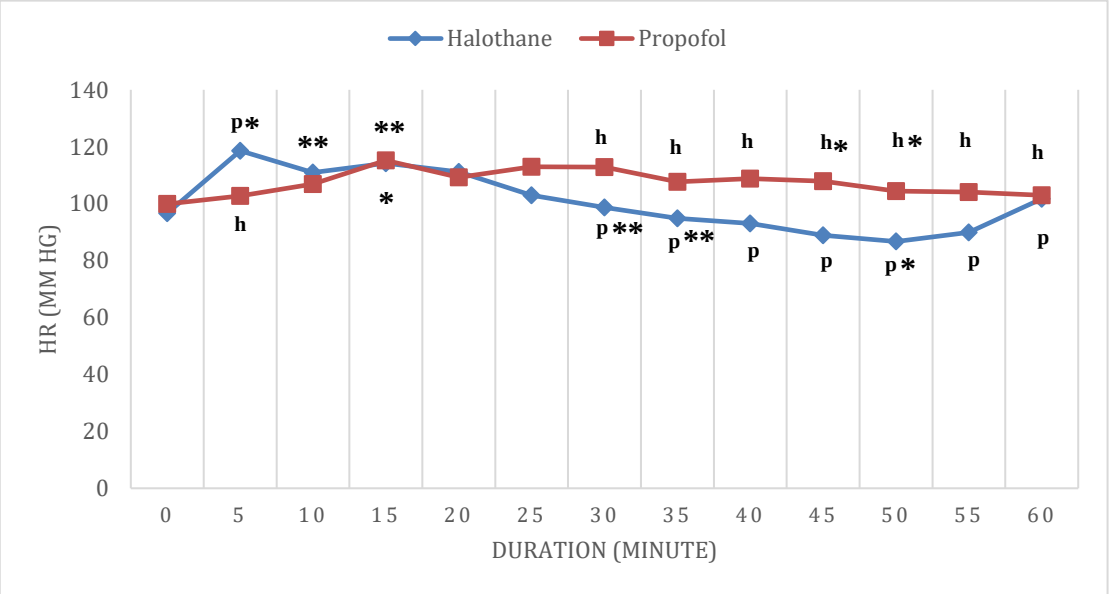


**Figure 4: Values of heart rate (HR) in cats under maintenance anesthesia with halothane and propofol. The mean S.D. is represented by each point and vertical bar (n=18).**

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

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

h, p: Differs significantly (p< 0.05) between the two groups at corresponding intervals.

### 4.2.2 Findings of the respiratory rate (RR)

There was a statistically significant difference (P＜0.01) in the respiratory rate of the HF group and the PF group at 30 and 35 minutes after the anesthetic was administered.

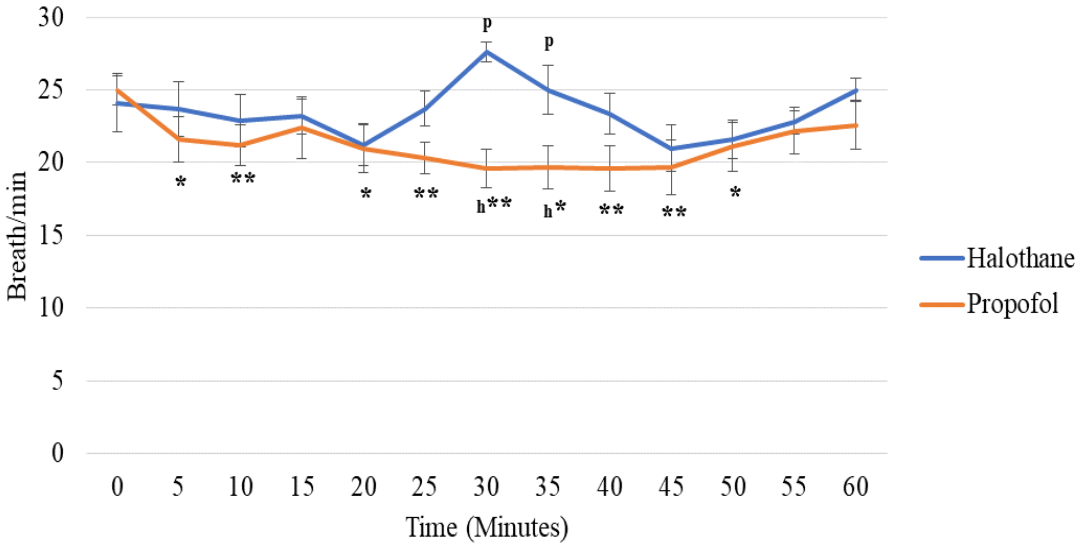


**Figure 5: Values of respiration rate (RR) in cats during halothane and propofol maintenance anesthesia. Each point and vertical bar represent the mean ± S.D. (n=18).**

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

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

h, p: Differs significantly (p< 0.05) between the two groups at corresponding intervals.

### 4.3 Findings of oxygen saturation ($SpO_2$)

There were no significant differences in $SpO_2$ between the two groups, beginning with the base value and continuing through all the subsequent values. (Figure 6).

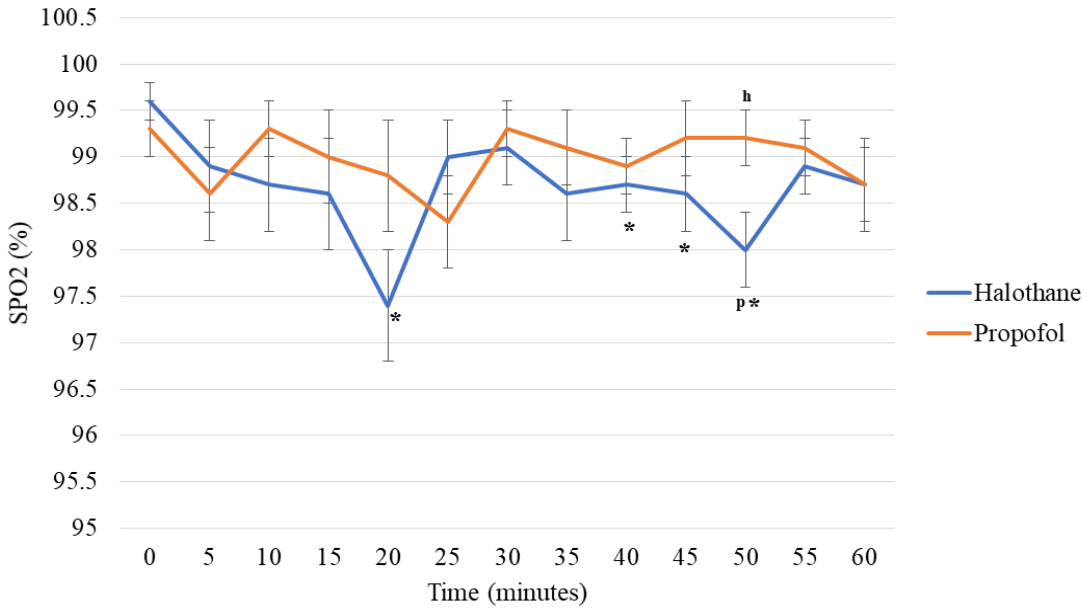


**Figure 6: Values of Oxygen saturation ($SpO_2$) in cats during halothane and propofol maintenance anesthesia. Each point and vertical bar represent the mean ± S.D (n=18). No significant differences were found between the two groups or from base value to other values.**

### 4.4 Findings of blood pressure

Figures 7, 8, and 9 show the mean ± S.D values of systolic (SAP), diastolic (DAP), and mean (MAP) arterial pressures in 18 cats.

#### 4.4.1 Systolic arterial pressures (SAP)

There was a statistically significant difference ($P < 0.01$) in the systolic arterial pressure of the HF group and the PF group from 20 to 55 minutes after the anesthetic was administered.

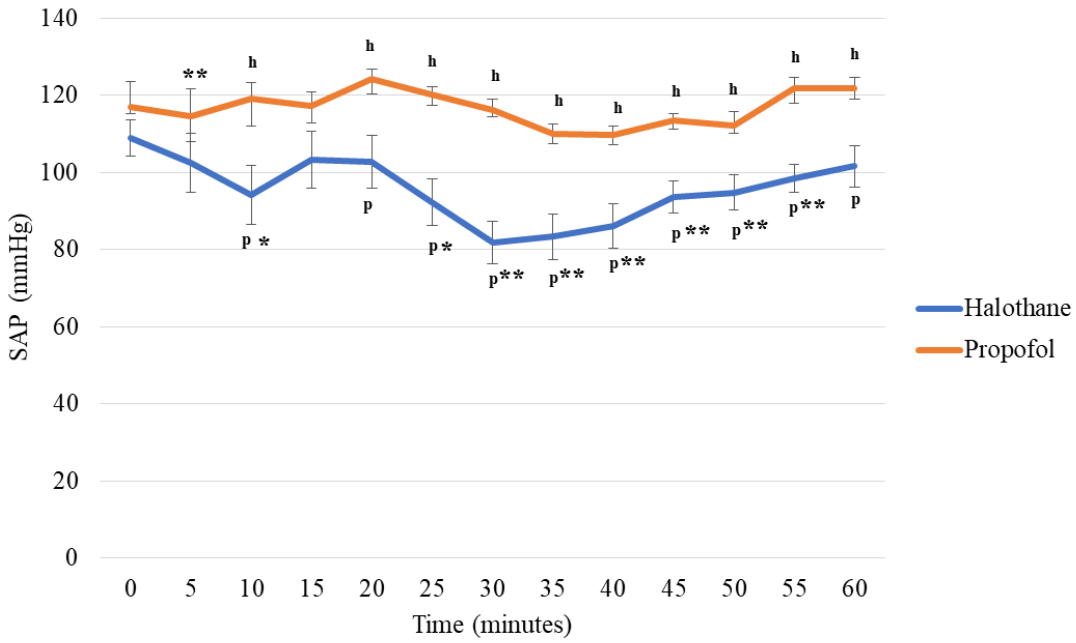


**Figure 7: Values of systolic arterial pressure (SAP) in CATS during halothane and propofol maintenance anesthesia. Each point and vertical bar represent the mean ± S.D. (n=18).**

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

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

h, p: Differs significantly ($p< 0.05$) between the two groups at corresponding intervals.

### 4.4.2 Diastolic arterial pressures (DAP)

There was a statistically significant difference ($P<0.01$) in the diastolic arterial pressure of the HF group and the PF group from 25 to 50 minutes after the anesthetic was administered.

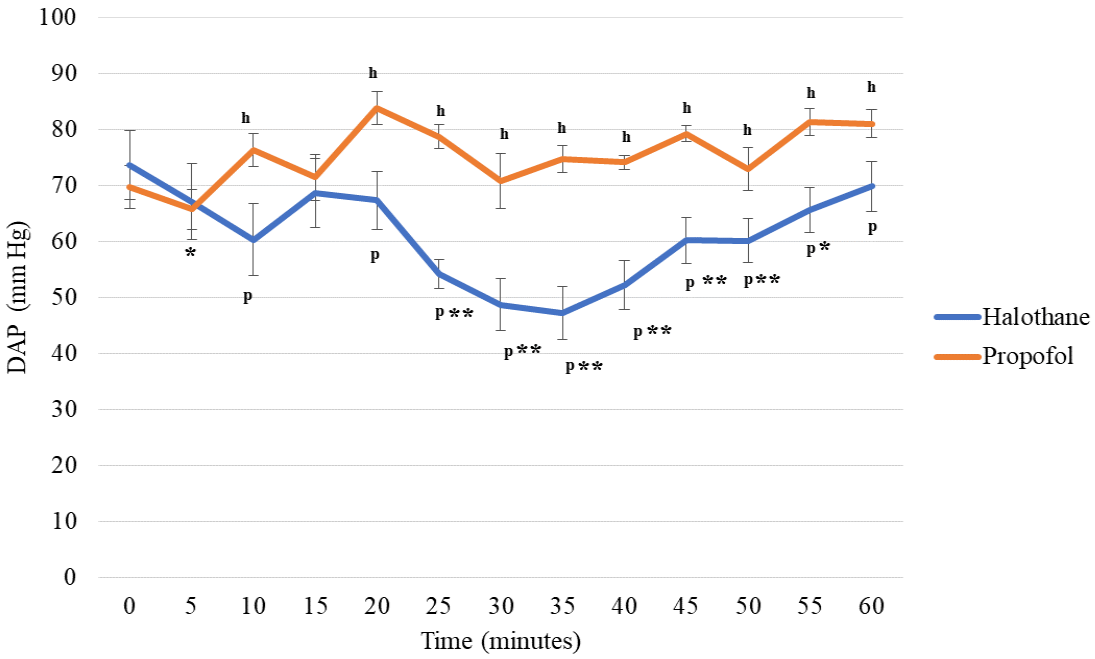


**Figure 8: Values of Diastolic arterial pressures (DAP) in CATS during halothane and propofol maintenance anesthesia. Each point and vertical bar represent the mean ± S.D. (n=18).**

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

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

h, p: Differs significantly ($p< 0.05$) between the two groups at corresponding intervals.

### 4.4.3 Mean arterial pressure (MAP)

There was a statistically significant difference (P＜0.01) in the mean arterial pressure of the HF group and the PF group from 25 to 55 minutes after the anesthetic was administered.

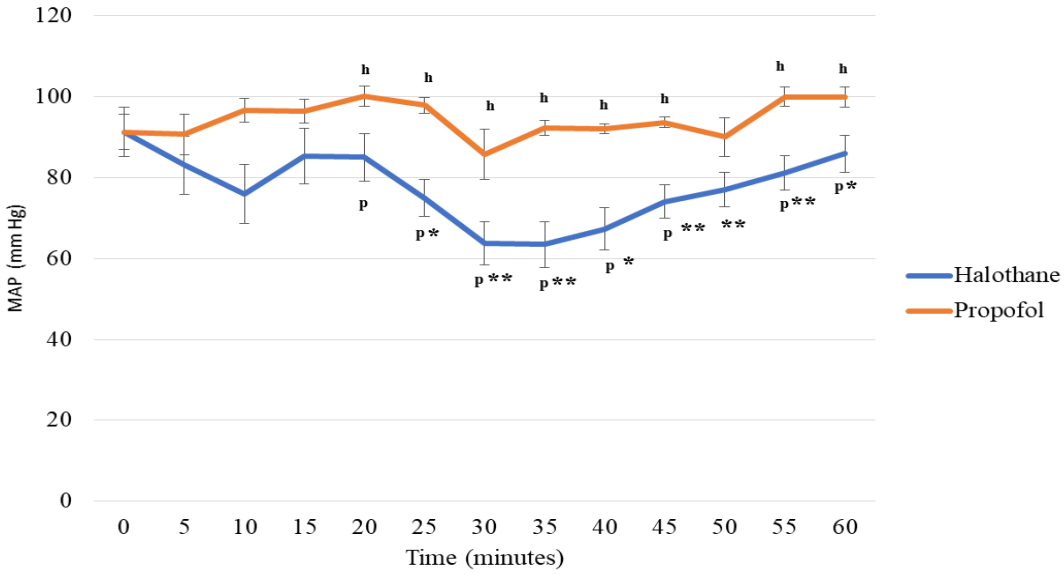


**Figure 9: Values of mean arterial pressures (MAP) in Cats during halothane and propofol maintenance anesthesia. Each point and vertical bar represent the mean ± S.D. (n=18).**

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

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

h, p: Differs significantly (p< 0.05) between the two groups at corresponding intervals.

### 4.5 $EtCO_2$ findings

There was not a significant change seen in either group; however, when comparing the two groups after 5 minutes, there was a significant difference (p＜0.05).

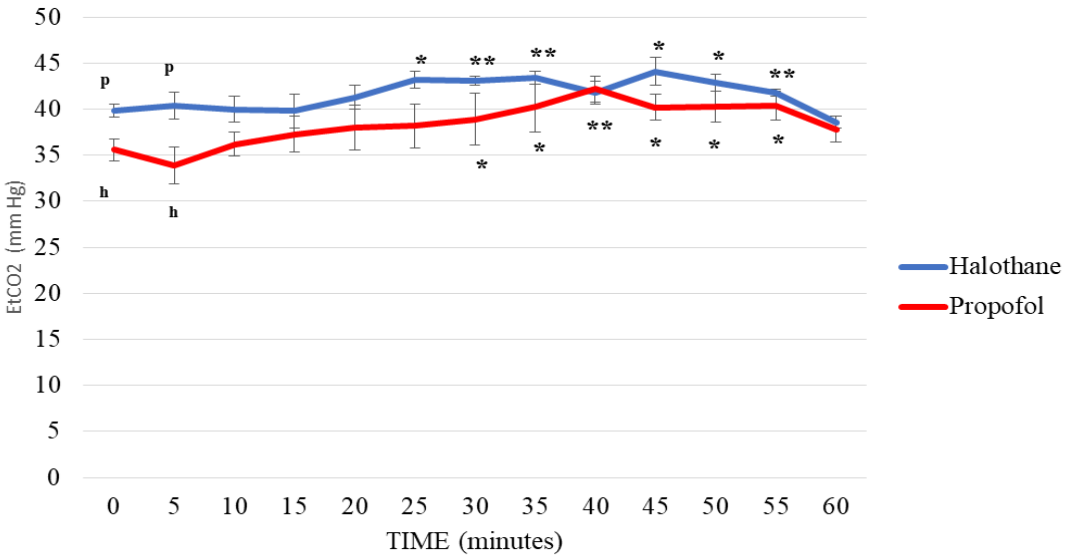


**Figure 10: Values of End-tidal $CO_2$ ($EtCO_2$) in Cats during halothane and propofol maintenance anesthesia. Each point and vertical bar represent the mean ± S.D. (n=18).**

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

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

### 4.6 Temperature

There was not a significant difference between the HF group and the PF group, although the PF group maintained the temperature more consistently in comparison to the base value.

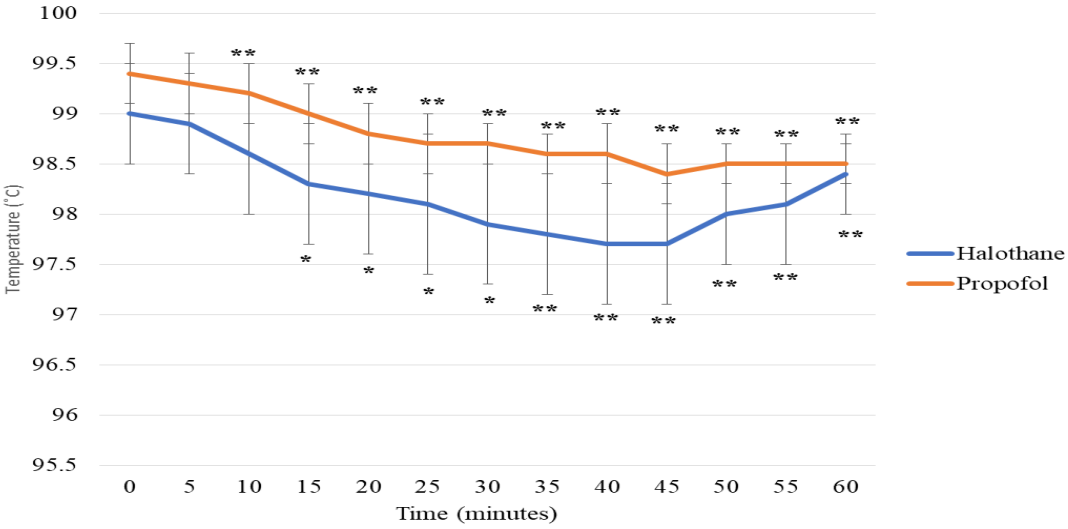


Figure 11: Values of Temperature in cats during halothane and propofol maintenance anesthesia. Each point and vertical bar represent the mean ± S.D. (n=18).

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

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

### 4.7 Anesthetic Requirements to Achieve an Acceptable Anesthetic Depth

During the surgical procedure, the observed mean FE0 halo was 1.5 – 2.5 % and the mean CRI of propofol was 10-11mg/kg/hour.

There were no statistical differences in either HF or PF protocols for anesthetic requirements from T0 to T6. All cats showed lack of palpebral and pedal reflexes, ventromedial rotation of the eye and relaxed muscular tone in the neck.

**Table 2: FE'Halo (%) of Halothane (PIVA) and milligrams (mg/kg/hour) administered during constant propofol infusion (TIVA), observed in cats undergoing ovary hysterectomy and receiving continuous infusion of fentanyl (0.002 mg/kg/h)**

| Groups | T0 | T1 | T2 | T3 | T4 | T5 | T6 |
|---|---|---|---|---|---|---|---|
| HF | 2% | 2% | 2.50% | 2.50% | 2.50% | 2% | 1.50% |
| PF | 10mg/kg/hour | 10mg/kg/hour | 11mg/kg/hour | 11mg/kg/hour | 11mg/kg/hour | 10mg/kg/hour | 10mg/kg/hour |

Cardiopulmonary variables did not differ significantly between PIVA and TIVA protocols (Table 3), except for SAP at surgical times T3, T5, and T6; at this time points, significantly higher values were observed during TIVA ($p = 0.0382$, 0.0398 and 0.0143, respectively).

**Table 3: Cardiopulmonary variables recorded in cats anaesthetized with either Halothane–fentanyl (HF) or propofol– fentanyl (PF) at T0 (before skin incision), T1 (during skin incision), T2 (during excision of left ovary), T3 (during excision of right ovary), T4 (During excision of uterus), T5 (during maintenance when surgery had commenced but when intense surgical stimulation was not present), T6 (at skin closure).**

| Parameter | Type of Anesthesia | Before skin incision T0 (Mean ± SD) | During skin incision T1 (Mean ± SD) | During excision of left ovary T2 (Mean ± SD) | During excision of right ovary T3 (Mean ± SD) | During excision of uterus T4 (Mean ± SD) | During maintenance when surgery had commenced but when intense surgical stimulation was not present T5 (Mean ± SD) | At skin closure T6 (Mean ± SD) |
|---|---|---|---|---|---|---|---|---|
| HR | HF | 96.6 ± 4.4 | 118.6 ± 13.4 *$^{p}$ | 114.2 ± 12.2* | 111.2 ± 27 | 103 ± 8.6$^{p}$ | 98.7 ± 8.4$^{p}$ | 94.8 ± 8.6$^{p}$ |
| | PF | 99.9 ± 8.7 | 102.7 ± 7.3$^{h}$ | 115.2 ± 9.6* | 109.3 ± 7.9 | 113 ± 9.9*$^{h}$ | 112.9 ± 8.6*$^{h}$ | 107.7 ± 9.9$^{h}$ |
| $SpO_2$ | HF | 99.6 ± 0.7 | 98.9 ± 1.5 | 98.6 ± 1.7 | 97.4 ± 1.9* | 99 ± 1.1 | 99.1 ± 1.4 | 98.6 ± 1.4 |
| | PF | 99.3 ± 1 | 98.6 ± 1.6 | 99 ± 1.5 | 98.8 ± 1.7 | 98.3 ± 1.6 | 99.3 ± 1 | 99.1 ± 1.2 |
| RR | HF | 24.1 ± 6 | 23.7 ± 5.8 | 23.2 ± 3.3 | 21.2 ± 4.1 | 23.7 ± 3.5 | 27.6 ± 2.1$^{p}$ | 25 ± 5.2$^{p}$ |
| | PF | 25 ± 3 | 21.6 ± 4.9* | 22.4 ± 6.4 | 21 ± 5.2* | 20.3 ± 3.3* | 19.6 ± 4*$^{h}$ | 19.7 ± 4.6*$^{h}$ |
| SAP | HF | 109 ± 14.1 | 102.4 ± 23.3 | 103.3 ± 22.3 | 102.7 ± 20.4$^{p}$ | 92.3 ± 18.1*$^{p}$ | 81.8 ± 16.5*$^{p}$ | 83.3 ± 17.8*$^{p}$ |

| Parameter | Type of Anesthesia | Before skin incision T0 (Mean ± SD) | During skin incision T1 (Mean ± SD) | During excision of left ovary T2 (Mean ± SD) | During excision of right ovary T3 (Mean ± SD) | During excision of uterus T4 (Mean ± SD) | During maintenance when surgery had commenced but when intense surgical stimulation was not present T5 (Mean ± SD) | At skin closure T6 (Mean ± SD) |
|---|---|---|---|---|---|---|---|---|
| | PF | 116.9 ± 20 | 114.6 ± 20.9* | 117.2 ± 11.2 | 124.1 ± 8.1$^{h}$ | 120.1 ± 6.1$^{h}$ | 116.3 ± 7.7$^{h}$ | 110.1 ± 7.4$^{h}$ |
| DAP | HF | 73.6 ± 18.3 | 67.1 ± 20.2 | 68.6 ± 18.7 | 67.3 ± 15.5$^{p}$ | 54.2 ± 7.9*$^{p}$ | 48.7 ± 14.1*$^{p}$ | 47.2 ± 14.4*$^{p}$ |
| | PF | 69.7 ± 11.7 | 65.7 ± 10.7* | 71.4 ± 12.2 | 83.8 ± 9.1$^{h}$ | 78.7 ± 6.3$^{h}$ | 70.7 ± 14.6$^{h}$ | 74.7 ± 7.1$^{h}$ |
| MAP | HF | 91.2 ± 18.3 | 83 ± 21.7 | 85.3 ± 20.7 | 85 ± 17.7$^{p}$ | 74.9 ± 13.7*$^{p}$ | 63.7 ± 16.2*$^{p}$ | 63.4 ± 17.2*$^{p}$ |
| | PF | 91.2 ± 12.8 | 90.6 ± 14.9 | 96.4 ± 8.7 | 100 ± 7.4$^{h}$ | 97.8 ± 5.8$^{h}$ | 85.7 ± 18.5$^{h}$ | 92.2 ± 5.7$^{h}$ |
| TEMP | HF | 99 ± 1.5 | 98.9 ± 1.6 | 98.3 ± 1.8* | 98.2 ± 1.8* | 98.1 ± 2* | 97.9 ± 1.9* | 97.8 ± 1.9* |
| | PF | 99.4 ± 0.9 | 99.3 ± 0.8 | 99 ± 0.8* | 98.8 ± 0.8* | 98.7 ± 0.8* | 98.7 ± 0.7* | 98.6 ± 0.7* |
| EtCO2 | HF | 39.8 ± 2.2$^{p}$ | 40.4 ± 4.4$^{p}$ | 39.8 ± 5.5 | 41.3 ± 4.1 | 43.2 ± 2.7* | 43.1 ± 1.5* | 43.4 ± 2.1* |
| | PF | 35.6 ± 3.5$^{h}$ | 33.9 ± 6.1$^{h}$ | 37.3 ± 5.7 | 38 ± 7.2 | 38.2 ± 7.2 | 38.9 ± 8.5* | 40.3 ± 8.5* |

*Significant difference ($p < 0.05$) to previous measurement within groups.

h or p Significant difference ($p < 0.05$) between groups at the same time or time period.

Data expressed as mean ± SD.

### 4.8 Anesthesia Recovery

Mean time to extubation was 9.6±1.5 and 14±1.3 min for HF and PF protocols ($p<0.01$), respectively. Mean time to first head lift was 14.6±1.9 and 22.7±3 min for PIVA and TIVA protocols ($p<0.01$), respectively. Mean time to sternal recumbency was 18.3±2.5 and 31±3.4 min for PIVA and TIVA protocols ($p<0.01$), respectively. Times to extubation, sternal position were significantly different between TIVA and PIVA protocols. The PIVA protocol takes less time than the TIVA protocol during recovery (figure 12).

Some abnormal behavioral signs, vocalization, restlessness was observed in PIVA group (n = 2) during the recovery period.

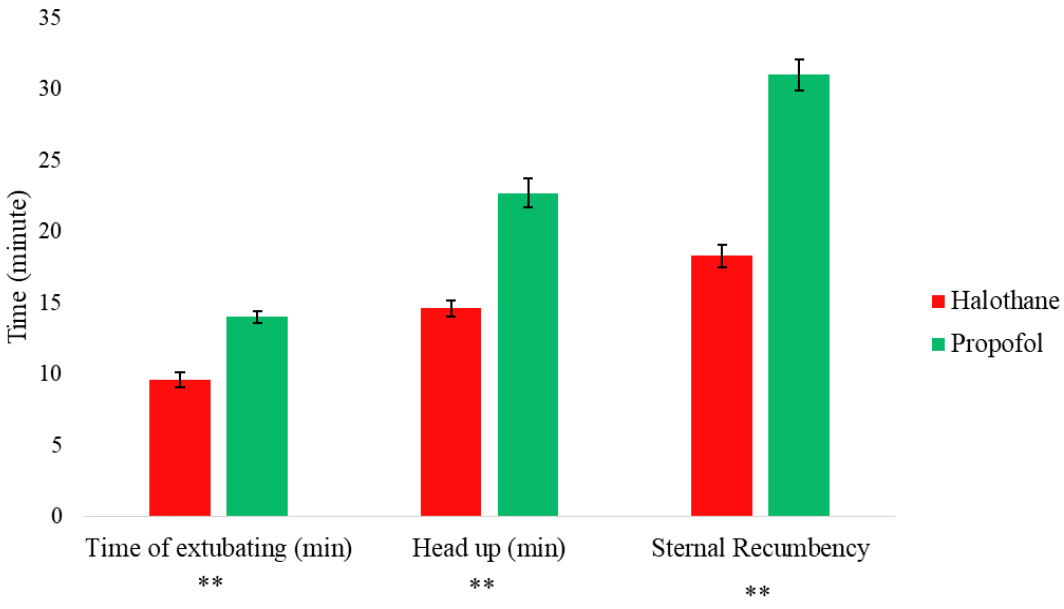


**Figure 12: Recovery data comparing halothane-fentanyl (HF) and propofol-fentanyl in cats. Each column represents the mean value with a vertical bar indicating S.D. (n=18).**

**: Significant difference between the anesthesia agents ($P < 0.01$).

Simple descriptive scale (appendix 4) used to measure the quality of recovery and Quality of anesthesia (Hunt et al., 2013) where there was no response from the stimulation in all the patient's undergoing ovariohysterectomy.

**Table 4: Summary of anesthesia and recovery quality, maintained with halothane-fentanyl and propofol-fentanyl**

| Categories | HF (n=9) | PF (n=9) |
|---|---|---|
| Quality of anesthesia | 3 (n=9) | 3 (n=9) |
| Pain assessment during anesthesia | 0 (n=9) | 0 (n=9) |
| Quality of recovery | 3 (n=7) | 3 (n=9) |
| | 2 (n=2) | |

# Chapter-V: Discussion

Analgesia prevents pain and suffering and is a crucial element of veterinary care. Neutering is an elective operation that causes discomfort to usually painless animals. Ovariohysterectomy is advised in dogs and cats to reduce reproductive behavior and illnesses. It may cause moderate to severe discomfort (Hardie et al., 1997) and is known to most veterinary doctors. By lowering the amount of peripheral and central sensitization, choosing the proper dose of perioperative analgesia for each specific treatment is critical to guaranteeing patient welfare and avoiding longer-term chronic pain syndromes (Woolf, 2011). Veterinary surgeons must have access to a wide spectrum of analgesics in order to do this.

The cats in this investigation were able to achieve a moderate level of drowsiness using the same dosage of xylazine (0.75/kg) as that employed by Selmi et al. (2005); Dzikiti et al. (2007) and Muir and Hubbell (2014) in their prior work. The use of sedative drugs facilitates restraint during the induction of anesthesia and reduces drug requirements for induction anesthesia and maintenance. In our study All patients were moderately sedated using dosage of xylazine @0.8mg/kg body weight (Robertson et al., 2018).

The mean propofol dose for anesthesia induction in the present study was 1 mg/kg, which is considerably lower than the doses reported in previous studies with non-premedicated cats (e.g., 6 mg/kg, (Mathis et al., 2012; Campagna et al., 2015); and 5 mg/kg, (Pascoe et al., 2006)). (Afolabi et al., 2019), also found the same result through the dose used in our study. (Robinson and Borer-Weir (2015) demonstrated that in premedicated cats the dose of propofol @2mg/kg is enough for induction. And there was another guideline that stated that the dose of propofol for induction is 2-6mg, but the dose should be reduced in premedicated and moderately sedated patients. In addition, sick, debilitated, or depressed patients may require lower doses than healthy, alert patients. Anesthetic induction is most effectively and efficiently achieved by IV administration of fast-acting drugs like propofol (Grubb et al., 2020).

When fentanyl is injected intravenously in cats, it is quickly eliminated, which makes it acceptable for usage in the peracute setting. This setting includes applications such as an adjuvant to the induction of anesthesia, neuroleptanalgesia, and intraoperative

analgesia. Fentanyl and its analogs do not alter blood pressure and systemic vascular resistance (Bovill et al., 1984; Ilkiw et al., 1997; Lee et al., 2000). Research has been done on the canine pharmacokinetics of fentanyl administered through CRI (Sano et al., 2006) and it was shown that the plasma concentration remained very steady after 4 hours without considerable buildup. In a study conducted on premedicated dogs by (Steagall et al., 2006), a reduction in the amount of isoflurane needed for anesthesia reached up to 54-66%, and in another study conducted on dogs, a drop in the amount of sevoflurane needed for anesthesia ranged between 22-41% (Reilly et al., 2013). The administration of fentanyl has been shown to cause respiratory depression and bradycardia. The vagally-mediated bradycardia that follows the administration of fentanyl may partially counteract the increase in blood pressure that occurs in response to a reduction in the amount of inhalant agent, and as a result, this condition needs to be treated with anticholinergics (Steagall et al., 2006). Patients under anesthesia frequently need intermittent positive pressure ventilation (IPPV) performed because of respiratory depression. The patients in our research did not need continuous positive airway pressure ventilation or intermittent positive airway pressure ventilation (IPPV).

It has been shown that ovariectomies, which include the removal of both the uterus and the ovaries, may cause moderate to severe pain in dogs, but ovariectomies usually induce moderate pain in cats (Hardie et al., 1997; Lascelles et al., 1999; Hellyer et al., 2007). This is in line with the degree of discomfort that has been experienced by women who have had abdominal hysterectomy (Perniola et al., 2014). In based upon the information presented above as well as the findings of the current research, it is plausible to hypothesize that ovariohysterectomy is an extremely painful procedure. This hypothesis could help to explain why a higher rate of propofol infusion was required in the previous study in order to achieve satisfactory levels of anesthesia (Smith, 1994). Because propofol does not have any impact on pain during unpleasant operations (such ovariohysterectomy), larger infusion rates are required in conjunction with analgesic medication but in this study, we maintain the propofol infusion at the lower margin with fentanyl cri (Liehmann et al., 2006).

In the present research, the average rate of propofol infusion that was required to adequately maintain anesthesia was 10 mg/kg/hour, which is lower than the rate that

was found in previous studies with premedicated cats. Afolabi et al. (2019) reported propofol infusion rates of 1.2mg/kg/hour, but Liehmann et al. (2006) reported infusion rates of 12mg/kg/hour for the drug. In all these trials, the decrease in the rate of propofol infusion that was required for the maintenance of anesthesia was caused by the administration of fentanyl at a rate of 0.002 mg/kg/hour. They are comparable to the dosage that was demonstrated to prevent a reaction to toe-pinch in 50 percent of cats (0.21 mg/kg/minute) (Ilkiw et al., 2003), and they are also equivalent to the dose that was used to prevent a response to a toe pinch in six cats (0.2-0.24 mg/kg/minute) (Mendes and Selmi, 2003). It is interesting to notice that the infusions in this more recent trial seemed to grow with time, whilst ours have remained the same.

All animals, regardless of species, will experience a dose-related decrease in their cardiopulmonary function after receiving inhalation anesthetic (Polis et al., 2001; Steffey, 2002). Anesthetics that contain halogens, such as halothane and isoflurane (Aguado et al., 2011), have the potential to alter the pace and rhythm of a patient's heartbeat (Nakaigawa et al., 1995). Halothane causes dose-dependent respiratory depression, leading to a progressive rise in $PaCO_2$. In our study EtCO2 was well maintained in all patients. Nevertheless, animals tend to breathe spontaneously better under halothane anesthesia than after the more modern agents (Steffey, 2002). Halothane has minimal muscle relaxant effects and is a poor analgesic, so supplementation with analgesics is often effective. In our study fentanyl was used as an analgesic agent where fentanyl CRIs were initiated with loading dose of fentanyl @0.005mg/kg followed by 0.002mg/kg/hour (Tranquilli et al., 2013).

The increased HR values that were observed over time (Table 3) may be the result of surgical stimulation and the subsequent activation of the sympathetic nervous system skin incision (T1) and its subsequent reinsertion (T4, T5, T6) when compared to the base value, although this is not certain. According to Hall and Clarke (2014), these increases did not surpass the physiological limits, which range from 120 to 140 beats per minute. During the operation, the SAP values of the HF were considerably lower than those of the TF at T3, T4, T5, and T6. Hall and Clarke (2014) found that halothane lowers vascular resistance after vasodilation, which results in a lower blood pressure reading for the patient. This distinction may be explained by this property of halothane. Nevertheless, SAP values in animals in the PF group were never lower

than those at the beginning of surgery (T0), which indicates that the requirements for propofol anesthesia were adequate during the surgical process because dose-related major cardiovascular depressive effects were not observed; however, a slight increase in HR values, along with a subsequent increase in blood pressure, were recorded up to T3-T6. On the other hand, the values of HR increased throughout this time period, whilst the values of blood pressure declined. It is highly likely that the rise in FE'Halo that occurs between T2 and T4 is responsible for this impact (Table 3). It appears that there is few information on the incidence of cardiac arrhythmias in cats and dogs while they are under the influence of halothane or any other kind of anesthesia (Cohen and Tilley, 1979). In human beings, the incidence ranges anywhere from 20 to 50 % (Katz and Bigger, 1970).

There was no apparent respiratory depression seen in cats subjected to either the TIVA or the PIVA treatment, as demonstrated by the average ET-CO2 (End tidal CO2) values that were measured. During anesthesia, hypercapnia is one of the factors that could potentially cause cardiac arrhythmias (Cohen and Tilley, 1979). In example, hypercapnia is responsible for a wide variety of unfavorable outcomes, such as depressed myocardial function and bradyarrhythmia (Hartsfield, 1996; Muir and Hubbell, 2014). In the course of our research, the Et-$CO_2$ level was never higher than 6.67 kPa (50 mm Hg).

Compared to the conventional method of blood gas analysis, pulse oximetry can report the blood's oxygen concentration in a way that more accurately reflects a patient's oxygenation status (Muir and Hubbell, 2014). An estimate of the percentage of the patient's hemoglobin saturated with oxygen can be obtained from the pulse oximeter ($SpO_2$). The measurement of $SaO_2$ is an invasive method that requires an arterial blood sample to determine hemoglobin saturation; therefore, monitoring the $SpO_2$ is an excellent alternative that provides an early warning of desaturation. $SpO_2$ is an indirect and non-invasive method of measurement of SaO2, which is an invasive method. The fact that the $SpO_2$ findings obtained in this study were above 95% in both HF and PF groups shows that the available hemoglobin in the blood was appropriately saturated with oxygen for the entirety of the time that the measurement was being carried out. The finding that was obtained by measuring the respiratory rate provided support for this theory.

The core temperature of the cats in the research did not go below 37 degrees Celsius, which is the threshold for hypothermia (Dhupa, 1995). Temperatures below 37℃ been linked to bradyarrhythmia and cardiac arrest (Moon and Ilkiw, 1993). Halothane can be a trigger for malignant hyperthermia, as can all the halogenated anesthetic agents (Hall, Clarke, et al., 2001). In our study there was no significant change in temperature between HF and PF groups. But the temperature is well maintained in the propofol-fentanyl group. Hypothermia caused by agonists of the beta 2-adrenoceptor is more likely to occur in cats than in dogs (Doherty, 1988). The hypothermia can be due to either a decrease in heat generation associated to the decrease in muscle activity or to a direct influence on the noradrenergic hypothalamic systems that are involved in thermoregulation. Both of these possibilities are possible explanations for the condition (Virtanen, 1989). In this study, similar drops in rectal temperature were observed in the HF group. The hypothermia observed in the present study was not significant as clinical hypothermia occurs below 35℃. However, the declines were probably minimized since the patients used a heating pad while they were undergoing surgery.

Recoveries were smooth, relatively fast, comparable, and significant between the two groups ($p<0.01$). During recovery, two of the cats in Group HF experienced seizures with vocalization. The experience lasted for about a minute and a half, and it ended once the cat was able to hide under a blanket and was no longer bothered by loud noises or bright lights. In the past, violent recoveries accompanied by seizures have been described with (Dodman, 1980). It was stated that these recoveries improved when the patient did not experience any discomfort and was allowed to remain in a setting that was calm, warm, and comfortable (Hall, Clarke, et al., 2001; Hall, Sandham, et al., 2001). In our study, there is less in HF group than in PF group. The incidence of delayed recovery following propofol infusion is higher in domestic cats than in domestic dogs. Cats have a longer elimination half-life for propofol than dogs do (Court, 2013). Recovery from anesthesia following propofol is dependent on redistribution and metabolism (Adam et al., 1980; Mathis et al., 2012). The difference in propofol metabolism between cats and other species may explain the longer recovery observed in our investigation. There have also been reports of pharmacokinetic variations in cats, with the prolonged elimination half-time reflecting a slower metabolism (Adam et al., 1980).

A simple descriptive scale was used in our study to evaluate pain response during anesthesia (Reid et al., 2013) and the quality of recovery, but simple descriptive scale is not likely to be able to measure all aspects of pain perception, especially in a veterinary setting (Holton et al., 1998). This scale is based on the experience of the assessor with pain behaviors and the worst pain that can happen during a certain procedure. Simple descriptive scale also cannot pick up on slight differences in pain that may be clinically important (Myles et al., 1999). However, by using this simple descriptive scale, the score was 0 in all our patients in both PF and HF group which could be one of the major limitations in our study.

We were able to use predetermined CRI dosages of fentanyl in our research design, which may not always be therapeutically appropriate. One of the drawbacks of our investigation was the absence of additional treated groups to further explain the sparing effect of each agent individually. In addition, this study only included cats that were classified as ASA 1 and were of the adult female variety. Due to the brief period that the study was conducted, the sample size was somewhat limited, and as a result, it does not accurately represent the entire population. The incorporation of sedative agents into the protocol may be seen as an additional constraint when it comes to the interpretation of cardiopulmonary data due to the number of effects that these agents have on anesthesia. However, Inhalation or intravenous anesthesia for domestic cats is difficult without sedatives. The experimental design targeted a lack of responsiveness to stimuli as acceptable depth of anesthesia; however, we did not adjust the fentanyl CRI to find an effective dosage that is another limitation of our study. In our study we use infusion pump to deliver drug, but multiple syringe pump device may be effective to deliver more than two drugs. Another limitation of our study was that the gaseous anesthetic machine to deliver halothane anesthetic was calibrated a long time ago. In our study Metabolic components (pH, HCO3, BE) were not assessed as blood gas analyzer was not available during the study period.

# Chapter-VI: Conclusions and Prospects

Our research leads us to conclude that propofol or halothane, used in TIVA or PIVA protocols respectively, combined with CRIs of fentanyl produced a satisfactory quality of anesthesia during surgery with minimal impact on cardiopulmonary function. However, cardiopulmonary values were well maintained in the propofol fentanyl group than the halothane-fentanyl group because the MAP value of the halothane fentanyl group was slightly lower than the propofol-fentanyl group. Nevertheless, recovery after anesthesia induced by the combination of propofol fentanyl takes more time than the halothane fentanyl group but the quality of anesthesia was better maintained in propofol fentanyl group. According to the findings of this research, either total intravenous anesthesia with propofol or halothane inhalation as partial intravenous anesthesia with Fentanyl CRI might be suitable options for the maintenance of anesthesia during ovariohysterectomy in domestic cats.

On the basis of our findings, we have come to the conclusion that fentanyl is the preferable alternative for analgesia during partial intravenous anesthesia and total intravenous anesthesia for ovariohysterectomy, and we anticipate that this will also be the case for other moderate to extremely painful surgical procedures. However, there are only a small number of studies that compare halothane and propofol. Additional studies can be conducted to compare other anesthetics with opioids in more painful soft tissue and orthopedic surgeries, and our study would provide additional information for the use of opioids in clinical practice.

# Chapter-VII: References


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# Appendix

## **Appendix**-I

Table: ASA physical status classification system (ASo, 2014)

| ASA PS Classification | Definition | Adult Examples, Including, but not Limited to: | Pediatric Examples, Including but not Limited to: | Obstetric Examples, Including but not Limited to: |
|---|---|---|---|---|
| **ASA I** | A normal healthy patient | Healthy, non-smoking, no or minimal alcohol use | Healthy (no acute or chronic disease), normal BMI percentile for age | |
| **ASA II** | A patient with mild systemic disease | Mild diseases only without substantive functional limitations. Current smoker, social alcohol drinker, pregnancy, obesity (30<BMI<40), well-controlled DM/HTN, mild lung disease | Asymptomatic congenital cardiac disease, well controlled dysrhythmias, asthma without exacerbation, well controlled epilepsy, non-insulin dependent diabetes mellitus, abnormal BMI percentile for age, mild/moderate OSA, oncologic state in remission, autism with mild limitations | Normal pregnancy*, well controlled gestational HTN, controlled preeclampsia without severe features, diet-controlled gestational DM. |
| **ASA III** | A patient with severe systemic disease | Substantive functional limitations; One or more moderate to severe diseases. Poorly controlled DM or HTN, COPD, morbid obesity (BMI ≥40), active hepatitis, alcohol | Uncorrected stable congenital cardiac abnormality, asthma with exacerbation, poorly controlled epilepsy, insulin dependent diabetes mellitus, morbid obesity, malnutrition, severe OSA, oncologic state, renal failure, muscular | Preeclampsia with severe features, gestational DM with complications or high insulin requirements, a thrombophilic disease requiring anticoagulation. |

| ASA PS Classification | Definition | Adult Examples, Including, but not Limited to: | Pediatric Examples, Including but not Limited to: | Obstetric Examples, Including but not Limited to: |
|---|---|---|---|---|
| | | dependence or abuse, implanted pacemaker, moderate reduction of ejection fraction, ESRD undergoing regularly scheduled dialysis, history (>3 months) of MI, CVA, TIA, or CAD/stents. | dystrophy, cystic fibrosis, history of organ transplantation, brain/spinal cord malformation, symptomatic hydrocephalus, premature infant PCA <60 weeks, autism with severe limitations, metabolic disease, difficult airway, long term parenteral nutrition. Full term infants <6 weeks of age. | |
| **ASA IV** | A patient with severe systemic disease that is a constant threat to life | Recent (<3 months) MI, CVA, TIA or CAD/stents, ongoing cardiac ischemia or severe valve dysfunction, severe reduction of ejection fraction, shock, sepsis, DIC, ARD or ESRD not undergoing regularly scheduled dialysis | Symptomatic congenital cardiac abnormality, congestive heart failure, active sequelae of prematurity, acute hypoxic-ischemic encephalopathy, shock, sepsis, disseminated intravascular coagulation, automatic implantable cardioverter-defibrillator, ventilator dependence, endocrinopathy, severe trauma, severe respiratory distress, advanced oncologic state. | Preeclampsia with severe features complicated by HELLP or other adverse event, peripartum cardiomyopathy with EF <40, uncorrected/decompensated heart disease, acquired or congenital. |
| **ASA V** | A moribund patient who is not expected to survive without the operation | Ruptured abdominal/thoracic aneurysm, massive trauma, intracranial bleed with mass effect, ischemic bowel in the face of significant cardiac | Massive trauma, intracranial hemorrhage with mass effect, patient requiring ECMO, respiratory failure or arrest, malignant hypertension, decompensated congestive heart failure, hepatic encephalopathy, | Uterine rupture. |

| ASA PS Classification | Definition | Adult Examples, Including, but not Limited to: | Pediatric Examples, Including but not Limited to: | Obstetric Examples, Including but not Limited to: |
|---|---|---|---|---|
| | | pathology or multiple organ/system dysfunction | ischemic bowel or multiple organ/system dysfunction. | |
| **ASA VI** | A declared brain-dead patient whose organs are being removed for donor purposes | | | |

** Although pregnancy is not a disease, the parturient' s physiologic state is significantly altered from when the woman is not pregnant, hence the assignment of ASA 2 for a woman with uncomplicated pregnancy.*

***The addition of "E" denotes Emergency surgery: (An emergency is defined as existing when delay in treatment of the patient would lead to a significant increase in the threat to life or body part)* (ASo, 2014).

**Appendix** II

**A questionnaire for surgery with gaseous anesthesia in small**

Case No. Case Reg. No. Date:

Owner name: Address: Mobile No:

Species: Breed: Age:

Sex: Body weight:

**Anamnesis/Clinical History:**

Previous illness:

Defecation: 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: ..... ℉

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:

**Appendix-III**

## Anesthesia Record Sheet

**Patient description:**

Date of registration: ID No: Species:

Breed: Age: Sex: Weight:

**Name of Surgery/Operation:**

**Pre-anesthetic evaluation of**

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

Other findings:

Surgeon:

Surgeon assistant:

Anesthesiologist:

| | 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/En | | | | | | | | | | | |
| Oxygenflow rate (L/min) | | | | | | | | | | | |
| $SpO_2$ % | | | | | | | | | | | |
| $EtCO_2$ mmHg | | | | | | | | | | | |
| Temperature ($^0F$) | | | | | | | | | | | |
| Cardiovascular parameters | 200 | | | | | | | | | | |
| | 180 | | | | | | | | | | |
| O Pulse/heart rate | 160 | | | | | | | | | | |
| V Systolic pressure | | | | | | | | | | | |

| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| = Mean pressure | 140 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| ∧ Diastolic pressure | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | 120 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | 100 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | 95 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | 85 | | | | | | | | | | | | | | | | | | | | | | | | | | : | | | |
| Respiratory rate × | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| (Breath/min) | 75 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | 65 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Intubated: Y / N | 55 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| ET tube size: | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| **Complications** | 45 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | 35 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bradycardia ( ) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Tachycardia ( ) | 25 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Hypotension ( ) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Apnea ( ) | 15 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Hypoventilation ( ) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Hypoxia ( ) | 5 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Anesthesia Depth Light/Medium/Deep | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| CRT (sec) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Fluid (ml given in 15min/Running total) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |

**Surgery time points**

| Parameter | Before skin incision | During skin incision | During excision of left ovary | During excision of right ovary | During excision of uterus | During maintenance when surgery had commenced but when intense surgical stimulation was not present | At skin closure |
|---|---|---|---|---|---|---|---|
| HR | | | | | | | |
| RR | | | | | | | |
| SAP | | | | | | | |
| DAP | | | | | | | |
| MAP | | | | | | | |
| $SPO_2$ | | | | | | | |
| $EtCO_2$ | | | | | | | |
| Pedal reflex | | | | | | | |
| Eye position | | | | | | | |
| CRT | | | | | | | |

**Recovery**

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

Head up …….. min,

Sternal recumbency……..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.

**Appendix IV**

Simple descriptive scale (SDS) (Reid et al., 2013)

| | |
|---|---|
| No pain | 0 |
| Mild pain | 1 |
| Moderate pain | 2 |
| Severe pain | 3 |
| Very severe pain | 4 |

## Biography

Dr. Sabiha Zarin Tasnim Bristi is the daughter of Abdul Hannan and Shahana Hannan. She is an MS Student of Surgery under the Department of Medicine and Surgery at Chattogram Veterinary and Animal Sciences University (CVASU). She successfully completed her DVM degree in 2018 from CVASU. She did her clinical training in veterinary clinical medicine at Tamil Nadu Veterinary and Animal Sciences University (TANUVAS), India and the Khon Kaen University, Thailand in the year 2018.At present she is working as a veterinary surgeon at people of animal welfare foundation, Bangladesh. She has immense interest to work for animal health and welfare. In particular, she envisions the plan to be engaged in further higher studies and research to contribute in the holistic approach of veterinary science finally to achieve a goal for the betterment of animal and human health. Her research and publications are based on veterinary surgery and anesthesiology. She has a great interest in veterinary anesthesiology.