ANAESTHETIC EFFICACY OF PROPOFOL AND KETAMINE-PROPOFOL ADMIXTURE WITH BUTORPHANOL AS CONSTANT RATE INFUSION USING FLUID BAG TECHNIQUE IN DOG

T H E S I S

Submitted
In partial fulfillment of the requirements for the Degree of

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BY
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DECLARATION OF STUDENT

I hereby declare that the experimental research work and interpretation of the thesis entitled **"ANAESTHETIC EFFICACY OF PROPOFOL AND KETAMINE-PROPOFOL ADMIXTURE WITH BUTORPHANOL AS CONSTANT RATE INFUSION USING FLUID BAG TECHNIQUE IN DOG"** or part there of has not been submitted for any other degree or diploma of any University, nor the data have been derived from any thesis/publication of any University or scientific organization. The sources of materials used and all assistance received during the course of investigation have been duly acknowledged.

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Declaration of advisory committee

BHAVE NEHA PRASAD has satisfactorily prosecuted her course of research for a period of not less than one semester and that the thesis entitled **"ANAESTHETIC EFFICACY OF PROPOFOL AND KETAMINE-PROPOFOL ADMIXTURE WITH BUTORPHANOL AS CONSTANT RATE INFUSION USING FLUID BAG TECHNIQUE IN DOG"** submitted by her is the result of research work is sufficient to warrant its presentation to the examination in the subject of **VETERINARY SURGERY AND RADIOLOGY** for the award of **MASTER OF VETERINARY SCIENCE** degree by the Maharashtra Animal and Fishery Sciences University, Nagpur.

We also certify that the thesis or part there of has not been previously submitted by her for a degree of any other University.

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CERTIFICATE

This is to certify that the thesis entitled **"ANAESTHETIC EFFICACY OF PROPOFOL AND KETAMINE-PROPOFOL ADMIXTURE WITH BUTORPHANOL AS CONSTANT RATE INFUSION USING FLUID BAG TECHNIQUE IN DOG"** submitted by **BHAVE NEHA PRASAD** to the Maharashtra Animal and Fishery Sciences University, Nagpur in partial fulfillment of the requirement for the degree of **MASTER OF VETERINARY SCIENCE** in **VETERINARY SURGERY AND RADIOLOGY** has been approved by the student's advisory committee after examination in collaboration with the External Examiner.

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Place: Akola **(Bhave Neha Prasad)**

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LIST OF ABBREVIATIONS

Abbreviation		Full form
%	-	Percentage
≥	-	greater than or equal to
±	-	plus/minus
µg	-	micrograms
@	-	at the rate of
<	-	lesser than
=	-	is equal to
>	-	greater than
µgm	-	micrograms
^{0}F	-	degrees of Fahrenheit
ALT	-	Alanine aminotransferase
AST	-	Aspartate aminotransferase
b.wt.	-	Body weight
BUN	-	Blood urea nitrogen
CRI	-	Constant Rate Infusion
cu.mm	-	cubic millimeters
dL	-	decilitre
DLC	-	Differential leucocyte count
e.g.	-	*exempli gratia*/for example
EDTA	-	Ethylenediaminetetraacetic acid
et al.	-	*et alia*/and others
Fig.	-	Figure
Hb	-	haemoglobin
hr	-	hour
IM	-	Intramuscular
inj.	-	injection
IU	-	International Units
IV	-	Intravenous
kg	-	kilograms
mg	-	milligrams
min	-	minute
ml	-	mililitre
n	-	Number of animals
p	-	probability
PCV	-	Packed cell volume
RBCs	-	Red Blood Cells
SC	-	Subcutaneous
SE	-	Standard Error
TEC	-	Total erythrocyte count
TLC	-	Total leucocyte count
viz.	-	namely
x	-	times
α	-	alpha

CHAPTER I

INTRODUCTION

Dogs are said to have evolved from the wolves and since then have been used for many purposes like, hunting, guarding and most importantly as a companion. Being a companion animal, they frequently require vet visits for their routine health check-ups or surgical procedures. Sometime female dogs undergo ovariohysterectomy procedure as a part of animal birth control programme which needs to be undertaken strictly under general anesthesia. Surgical management of canine patients is considered to be painful and require an ideal anesthetic which produces sleep, amnesia, analgesia and muscle relaxation to facilitate well-being of the surgical patient (Slingsby and Pearson, 2000). The ideal procedural anesthetic protocol is intended to have a short onset and recovery and to result in a depressed level of consciousness and analgesia with adequate cardiovascular and respiratory function (Aoud *et al.,* 2008). To obtain the efficient anesthetic efficacy, combination of two or more drugs to be preferred in veterinary practice called as balanced anesthesia.

Till today, inhalation agents have remained the routine choice for maintenance of anesthesia. However the principle requirement is the availability of sophisticated delivery system for gaseous and volatile anesthetic, which allows the anesthetist to have a fine degree of control on the concentration administered to the patient. The non-availability of sophisticated anesthetic machine and necessary equipment to administer inhalant anesthetic in the field makes its use practically unfeasible for the field veterinarians. Under field conditions intramuscular or intravenous anesthesia is usually the method of choice, as it can be performed with limited facilities at hand in animal hospital (Kumar *et al.,* 2014)

In the present scenario clinicians are using different anesthetic protocols including inhalant anesthesia, TIVA (Total Intravenous Anesthesia), local anesthesia etc. Local anesthesia includes local infiltration of local analgesic drug with or without sedation. This may sometimes cause breakdown of pain cycle due to short acting effect of drugs and may create patient discomfort. On the other hand, TIVA has become famous amongst the veterinary practitioners due to easy way of use and requirement of minimal instrumentation. TIVA (Total Intravenous Anesthesia) is a technique of general anesthesia that uses anesthetic agents given solely by the intravenous route and in the absence of all inhalation agents. Sophisticated and expensive instrument set-up of inhalation anaesthesia can be avoided which makes the procedure cost effective as well. Also the use of TIVA prevents the contamination of the operation theatre environment. It involves the delivery of a bolus dose or a fast loading infusion to achieve an adequate blood concentration of the anesthetic drug (Saikia *et al.,* 2016).

Constant Rate Infusion (CRI) includes constant infusion of an analgesic or anaesthetic drug through a volumetric infusion pump or syringe driver which maintains the constant plasma concentration of the particular drug. It masks the effects caused by the peaks and valleys caused due to intermittent bolus administrations leading to fewer sudden hemodynamic changes, lower total amount of anesthesia to be given and more rapid recovery from anesthesia. CRI can be performed by using a simple Fluid Bag Technique or using automated syringe pumps. Many drugs have been used in veterinary practice by CRI which includes morphine, fentanyl, ketamine, propofol, lidocaine etc. for anesthesia, post-operative pain management and peri-operative complications as well. Among these, propofol and ketamine have proved to be very effective for major or minor surgical procedures or outpatient diagnostic procedures which require light degree of sedation.

Any drug to be used by constant rate infusion should have properties which include a relatively short duration of action (Hall and Chambers, 1987). When these drugs are used as infusion after a bolus administration for induction, they maintain a steady plasma drug concentration throughout the anesthesia. For balanced anesthesia, an appropriate selection of pre-anesthetic drugs can significantly improve intra-operative cardiovascular stability, peri-operative analgesia and the quality of recovery (Waelbers *et al.,* 2009 and Saikia *et al.,* 2016). Therefore when an opioid drug is used in combination with propofol, it gives the patient sedation as well as profound analgesia which is lacked by propofol alone. If ketamine is added to the anesthetic protocol, it causes stabilization of cardio-vascular and respiratory systems which may be hampered by using propofol and an opioid.

Propofol is a newer generation injectable anesthetic agent introduced into veterinary practice in the 1990's. In dogs, it is characterized by rapid onset, short duration, easy titration, rapid clearance, lack of accumulation, rapid and smooth recovery and some degree of respiratory depression (Tsai *et al.,* 2007). Propofol (2,6-diisopropylphenol) is a non-barbiturate, non-opioid sedative-hypnotic intravenous agent. It is rapidly redistributed from the brain to other tissues and is also efficiently eliminated from plasma by hydroxylation by one or more hepatic cytochrome P-450 isoforms, which explains its short action and the rapid recovery (Zoran *et al.,* 1993). Onset of reaction is very quick of about 20-30 seconds and recovery period varies between 5-10 minutes with the elimination half-life of 1.4 hours in dogs. Due to these pharmacokinetic properties, it is a suitable drug for the maintenance of anesthesia by constant rate infusion. Excitatory effects and involuntary movements are observed occasionally in dogs during induction and recovery. Propofol does not affect hepatic or renal functions. It lacks the analgesic property, hence it is better to combine it with an opioid analgesic drug during major surgical procedures.

Ketamine, a phencyclidine hydrochloride derivative which is a non-competitive dissociative injectable anesthetic and potent noncompetitive antagonist at N-methyl-D-aspartate receptor. Ketamine is considered to be an extremely versatile agent as it can be administered by both IV and IM route without much tissue irritation. It induces a state called 'dissociative anesthesia' which is associated with intense feelings of dissociation from the environment. It exerts majority of its CNS actions by inhibiting the NMDA receptors and induces a cataleptic state. It produces sedation, amnesia and analgesia and has anticonvulsive properties. Following IV administration, ketamine produces rapid anesthesia (45-60 seconds) which lasts for about 10-60 minutes which is dose dependent. It has many advantages including cardiac stability, preservation of the respiratory rate and analgesic properties and hence can be used in the cases of hypotension or bradycardia. It is commonly used in many species and is famous for its use as it helps to reduce post-operative pain. It causes minimal cardiovascular depression, does not depress laryngeal, pharyngeal, corneal or palpebral reflexes and depresses ventilation less than other anesthetics or analgesics.

Ketamine and propofol, these two completely different anesthetics compensate each other's deficits due to their opposing physiological effects, when administered together. The side effects of propofol are largely dose-related, and it would be therefore advantageous to combine propofol with other anesthetic agents in order to decrease the dose, and minimize these adverse effects (Intelisano *et al.,* 2008). The opposing haemo-dynamic and respiration effects of propofol and ketamine may enhance the utility of this drug combination, increasing both safety and efficacy and allowing reduction in the dose of propofol alone required to achieve sedation (Daabis *et al.,* 2009). They are compatible at 23 degree celcius with no increase in particle content at site of injection (Trissal *et al.,* 1997). Clinical experience suggests that the use of ketamine-propofol combination has some advantages such as limited incidence of propofol induced respiratory depression, provision of analgesia from ketamine (Tobias, 2014) and decrease the cardio-respiratory side effects over using ketamine or propofol alone (Mair *et al.,* 2009). Also, the cardiovascular effects of each are opposing in action, thus balancing each other out when used together (Arora, 2007).

Butorphanol is partial opioid agonist which acts at kappa and sigma receptors. It is one of the most widely used analgesics and anesthetic adjuvants in veterinary medicine. It exhibits 4-7 times potency than morphine. It is used as a premedicant, analgesic, antitussive and antiemetic in dogs and cats. Its agonistic activity is thought to be exerted primarily at the kappa receptors. Adverse effects mainly include excitement, respiratory depression, ataxia, anorexia or diarrhea, which are less severe. This drug can be used in conjunction with propofol as constant infusion for perioperative analgesia.

Considering the strengths and weaknesses of CRI, amount of drug needed, quality of anesthesia, smooth recovery from anesthesia this study was planned with following objective.

Objective

- To evaluate the anaesthetic efficacy of propofol and ketamine-propofol Admixture with butorphanol as constant rate infusion using fluid bag technique in dog.

CHAPTER II

REVIEW OF LITERATURE

The present study deals with the evaluation of anaesthetic efficacy of propofol and ketamine-propofol admixture with butorphanol constant rate infusion using fluid bag technique as general anesthetic in dogs. The literatures regarding the study have been reviewed as under.

2.1 Assessment of Anaesthasia

2.1.1 Quality of anesthesia

Hall and Chambers (1987) conducted an experiment on 40 dogs presented for various diagnostic, major and minor surgical procedures, which were divided into 4 equal groups. All the dogs were premedicated with Inj. acepromazine @ 0.5 mg/ kg b.w and Inj. atropine @ 0.02 mg / kg b.w. Dogs in group I, II and III were induced with Inj. propofol @ 3 mg/kg IV as a bolus over 20 seconds and further incremental doses were given till jaw relaxation for intubation was evident. These dogs were maintained with 0.3, 0.35 and 0.4 mg/kg/min of propofol infusion. In group IV intubation was undertaken after induction with 1.25 or 2.50 per cent solution of thiopentone and maintained with nitrous oxide/halothane/oxygen mixture via standard non-rebreathing anesthetic circuit. They observed that the induction of anesthesia prior starting of infusion with a bolus dose had a disadvantage that the blood concentrations of the drug decreases below the desired concentration after the peak associated with the induction dose. They concluded that an infusion rate of 0.40 mg/kg/min of propofol produced surgical anesthesia in dogs and did not cause any marked respiratory depression.

Keegan and Greene (1993) studied the quality of anesthesia in terms of induction for a continuous two hour propofol infusion in six adult healthy mixed breed dogs. They were randomly divided into two groups receiving either propofol or isoflurane anesthesia. Dogs from propofol group were induced @5 mg/kg IV administered over 30 seconds. They observed that induction of anesthesia with propofol was consistently rapid and smooth and muscle tremors were not observed in any of the dogs. They emphasized on the need of preoxygenation and mechanical ventilation during anesthesia of propofol to avoid the episodes of apnea and cyanosis.

Nolan and Reid (1993) studied the pharmacokinetics of constant rate infusion of propofol in six Beagle dogs who underwent different surgical procedures. The dogs were premedicated with acepromazine @ 0.05 mg/kg and papaveretum at 0.4 mg/kg. They were induced with bolus of Inj. propofol @ 4 mg/kg. One minute after induction infusion of propofol was started at 0.4 mg/kg/min through an infusion pump. They observed that it took a period of 10 minutes to achieve the desired concentration of propofol after bolus administration and starting of infusion. Clinically all animals were in light plane of anesthesia although no movement was observed during the procedure. They also stated that a brisk palpebral reflex was present for the first 30-40 mins of infusion and occasional blinking was also spotted. They concluded that a combination of bolus and continuous infusion of propofol helped to achieve surgical anesthesia within 20 mins in all dogs.

Correia *et al.* (1996) conducted an experiment in five Scottish blackface sheep undergoing surgery for the implantation of subcutaneous tissue pouches to investigate the pharmacokinetic effects of propofol infusion alone or with ketamine. All sheep were premedicated with Inj. acepromazine @ 0.05 mg/kg and papaveretum @ 0.4 mg/kg intramuscularly. Anesthesia was induced in Group 1 with propofol at 4 mg/kg intravenously over 60 seconds and was maintained with a variable infusion rate of propofol at 0.3-0.5 mg/kg/min. While in Group A anesthesia was induced with propofol at 3 mg/kg mixed together with ketamine at 1 mg/kg intravenously and maintained with variable infusion rates of propofol 0.2-0.3 mg/kg/min and ketamine at 0.1 to 0.2 mg/kg/min separately. Infusions were administered by two volumetric infusion pumps. They observed that no purposeful movements were made by the patients during anesthesia and degree of analgesia appeared satisfactory.

Hellebrekers *et al.* (1998) compared the two anesthetic protocols i.e. medetomidine with propofol and medetomidine with ketamine. Total eighty four dogs were included in the study which were divided into two groups for different surgical and non-surgical procedures. All dogs were sedated with medetomidine and anesthetized with propofol in one group and with ketamine in second group. They observed that after onset of anesthesia the muscle tone of the jaw was greatly reduced in both the groups. They also mentioned that, side effects of anesthesia with propofol was characterized by initial respiratory depression, vomiting in some dogs, however there were no significant difference between the incidences of adverse reactions in both the groups.

Hughes and Nolan (1999) conducted an experimental study in eight adult Greyhound dogs to study the pharmacokinetic studies of propofol and fentanyl infusion. The dogs were premedicated with acepromazine @0.05mg/kg, 3-45 minutes before induction. Induction was carried out with propofol @4mg/kg as IV bolus and then infusion was started immediately. Incremental doses were given until intubation of the trachea was possible. Dogs A and B received propofol infusion @0.4mg/kg/min for 20 minutes which was reduced to 0.3mg/kg/min for further 70 minutes. Dogs C to H received an initial infusion of 0.3mg/kg/min for 20mins and 0.2mg/kg/min for further 70 mins. Fentanyl infusion was commenced in Dogs A and B @0.5µg/kg/min, Dog C at 0.3µg/kg/min and Dogs D to H at 0.1µg/kg/min. Propofol infusion rate was increased by 0.1mg/kg/min in dogs in which anesthesia was assessed as being light. Anesthetic depth was assessed by observing palpebral reflexes, jaw muscle tone, flexor withdrawal reflex, swallowing and voluntary limb movement. They observed that quality of anesthesia was satisfactory in all the dogs however the dogs were in the light plane of anesthesia. They concluded that, in presence of surgical stimulus, the infusion rates of the drugs mentioned earlier may need to be increased. They concluded that propofol when used as a sole anesthetic agent does not provide satisfactory anesthesia and induces cardiovascular and respiratory depression when used in doses required to prevent physical responses to major surgery.

Waelbers *et al.* (2009) reviewed the Total Intravenous Anesthasia in dogs. They mentioned that infusion techniques help achieve a more stable plane of anaesthasia which in terms of total amount of drug used is more economical. They also suggested that an appropriate selection of pre-aneasthetic drug is important to improve cardiovascular stability and intraoperative analgesia. They stated that propofol induces rapid, smooth induction and has a rapid redistribution from brain to other tissues and therefore considered to be a suitable drug for the maintenance of anesthesia by continuous rate infusion. Though it does not have an analgesic property, when used in conjunction with a potent analgesic drug it proves to be a good drug for CRI. They also emphasized that recovery in dogs can be prolonged after CRI of propofol exceeding 30 minutes. The combination of ketamine with a benzodiazepine can be used in premedicated dogs for procedures taking less than an hour to avoid the chances of muscle movements and convulsions.

Amin and Atiyah (2014) evaluated the general anaesthasia induced by propofol, ketamine protocol in rabbits premedicated with diazepam. Total seventeen rabbits were premedicated with diazepam at 1mg/kg b.wt intramuscularly and then induced with propofol at 10mg/kg intravenously and ketamine at 25 mg/kg intramuscularly. The quality of anaesthasia was judged by the depth of anaesthasia and muscle relaxation. They observed that the eye reflexes (palpebral and corneal) were never abolished. Muscle relaxations was achieved after premedication with diazepam which was thought to be due to depression of polysynaptic musculoskeletal reflexes. The depth of anaesthasia was characterized by no responding to painful stimulation, however still had corneal reflex. They mentioned that propofol in clinical doses was weak at controlling pain and had no analgesic properties, unless combined with analgesic drug.

Njoku (2015) carried out an experiment in eight adult mongrel dogs to study the quality of analgesia and anesthesia two anesthetic protocols. All the dogs were premedicated with atropine sulphate (at 0.03mg/kg bwt) and xylazine (at 2mg/kg bwt) and induction of anesthesia was carried out with ketamine at 2.5 mg/kg bwt and propofol at 4mg/kg bwt. The result of this study showed that pedal reflexes in both the groups reduced significantly ($p<0.05$) between the 10^{th}, 30^{th} and 60^{th} min post-induction, however there was no significant difference between the groups.

2.1.2 Recovery time

Morgan *et al.* (1990) studied the pharmacokinetics of propofol infusion in seven human patients undergoing major oral or neck surgery with reference to the recovery time. The patients were pre-anesthetized with temazepam or morphine and propofol was administered by intravenous infusion. They observed that whether administered by bolus or by continuous administration, the systemic clearance of propofol is lower and the elimination half-life is longer. They concluded that while calculating the infusion doses, this property of propofol should be taken into account to avoid accumulation of propofol into body tissues and hence resulted in prolonged recovery.

Nolan and Reid (1993) carried out constant rate infusion of propofol in seven beagle dogs which were undergoing surgery for implantation of subcutaneous tissue pouches. They observed that recovery after anesthesia was rapid in all dogs. They also stated that longer infusion of the propofol may result in delayed recovery because of accumulation of the propofol in the tissue stores.

Correia *et al.* (1996) conducted an experiment in five Scottish blackface sheep undergoing surgery for the implantation of subcutaneous tissue pouches to investigate the pharmacokinetic effects of propofol infusion alone or with ketamine. All sheep were premedicated with Inj. acepromazine @0.05mg/kg and papaveretum @ 0.4mg/kg intramuscularly. Anesthesia was induced in Group 1 with propofol at 4mg/kg intravenously over 60 seconds and was maintained with a variable infusion rate of propofol at 0.3-0.5mg/kg/min. While in Group A anesthesia was induced with propofol at 3mg/kg mixed together with ketamine at 1mg/kg intravenously and maintained with variable infusion rates of propofol 0.2-0.3mg/kg/min and ketamine at 0.1 to 0.2mg/kg/min separately. Infusions were administered by two volumetric infusion pumps. They observed that recovery from anesthesia was rapid and free of excitement in all the animals in both the groups. Although the animals in Group 2 took significantly longer to achieve sterna recumbency than those in Group 1.

Nolan *et al.* (1996) studied the pharmacokinetic effects of infusions of propofol and ketamine in ponies. For the experiment, four ponies were selected which were premedicated with detomidine at 20µg/kg. Anesthesia was induced with ketamine at 2.2mg/kg b.wt. intravenously. A bolus dose of propofol 0.5mg/kg b.wt was then administered intravenously and propofol and ketamine infused for 60 and 45 minutes respectively. The average infusion rate for propofol was 0.136mg/kg/min and for ketamine it was maintained at 50µg/kg/min. They observed that the recoveries of the ponies were proved to be satisfactory. They concluded that combination of propofol and ketamine administered together is suitable because of their rapid clearance from body.

Hellebrekers *et al.* (1998) conducted a study on dogs to compare the suitability of combination of medetomidine and propofol and medetomidine and ketamine for different surgical procedures. For the study, the used 84 dogs of either sex divided in four groups for different surgical and non-surgical processes. Anesthesia was induced either with propofol @ 2.1mg/kg body wt. or ketamine @@3.7g/kg body wt. They studied that in propofol group 89 per cent of the recoveries were smooth and only 4.50 per cent of the recoveries were characterized as restless. In contrast, in the ketamine group only 63 per cent of the recoveries were smooth and 37 per cent were regarded as restless.

Hughes and Nolan (1999) carried out total intravenous anesthesia in Greyhounds to study the pharmacokinetics of propofol and fentanyl. The study included eight Greyhounds which were premedicated with acepromazine at 0.05mg/kg b.wt. intramuscularly. Anesthesia was induced with a bolus of propofol at 4mg/kg b.wt. intravenously and infusion was begun. Five minutes after anesthesia, fentanyl (2µg/kg) and atropine sulphate (0.04mg/kg) were administered and fentanyl infusion begun. Propofol infusion lasted for 90 mins and fentanyl infusion for 70 min. They observed that recovery times were longer (mean time to head lift was 52 ± 12 min). They concluded that total intravenous anesthesia maintained with propofol and fentanyl infusion induced satisfactory anesthesia. Although considering the respiratory depressing effects of opioids and propofol, administration of atropine sulphate in necessary.

Pascoe *et al.* (2006) carried out an experiment in cats to determine the time required for recovery after constant infusion of propofol. All cats underwent anesthesia induced with propofol at 5mg/kg/min i.v bolus and then maintained with constant infusion at 0.4mg/kg/min for 30 mins in T30 group and for 150 min in T150 group. They observed that the initial time taken to lift the head in T150 group was longer when compared to the induction dose or T30 group. They concluded that if higher doses of propofol are administered for shorter periods or longer infusion times were used, the recovery was likely to be extended. They recommended that propofol infusion rate and duration should be minimized if this technique is used for maintenance of anesthesia in cats.

Tsai *et al.* (2007) demonstrated total intravenous anesthesia in 58 dogs undergoing different surgical procedures using propofol and compared it with isoflurane anesthesia. They observed that recovery from the propofol anesthesia was characterized by minimal amount of struggling, vocalization and excitement and required little or no physical restraint. They stated that most of the cases exhibited post-operative hypersalivation after propofol administration which was not premedicated with atropine sulphate and this hypersalivation was not related to post-operative pain. They concluded that propofol TIVA provides slower as well as smoother recovery and continuous dosing of propofol to canine patients will not predispose them to neurological signs when compared to induction with propofol and maintenance with isoflurane. Also, adverse effects including hypersalivation, neurologic excitement (paddling, muscle twitching, opisthotonus), vomiting/retching were observed in similar frequencies in both the protocols.

Ambros *et al.* (2008) studied the anesthetic efficacy of continuous rate infusion of alfaxalone-2-hydroxypropyl-beta-cyclodextrin and propofol in dogs. The experiment was conducted on six adult crossbred dogs who were divided into two equal groups. Each dog was sedated with acepromazine at 0.02 mg/kg IV and hydromorphone at 0.05mg/kg IV. Anesthesia was induced with propofol at 4mg/kg bwt or alphaxlone-HPCD at 2mg/kg bwt. Maintenance was done with the same treatment drugs i.e. propofol at 0.25mg/kg/min and alphaxalone-HPCD at 0.07g/kg/min for 120 mins. They observed that quality of recovery was similar with both the anesthetics and considered excellent overall. They concluded that preanesthetic medication and duarion of CRI influences the duration of recovery from anesthesia.

Njoku (2015) studied the physiological and anesthetic parameters of dogs anesthetized with ketamine and propofol and then maintained with either boluses of propofol or constant rate infusion of propofol. In the present study, recovery time was measured from the time of the last administration of propofol and the dog's ability to stand. He mentioned that recovery time from propofol anesthesia was dependent on the rate of propofol infusion and duration of maintenance of anesthesia. In this study, he observed the prolonged recovery time which was thought to be the result of long duration of maintenance of anesthesia (60 min) and possibly post-anesthetic sleep. He also suggested that pharmacokinetics of propofol in dogs was similar when administered intermittently or as constant infusion. The plasma concentration of propofol was above the required level in repeat boluses group than in constant infusion group where it was steady throughout the procedure.

Sharma *et al.* (2016) conducted a study in 100 human patients of either sex undergoing short orthopaedic procedures to compare the sedoanalgesic properties of the total intravenous infusion of mixture ketamine-propofol(ketofol) and fentanyl-propofol (fentofol). For the study, both fentofol and ketofol was prepared in 1:1 ratio and used for the maintenance of anesthesia by continuous infusion at the rate of 20ml/hr or more. Induction of anesthesia was achieved by administrating bolus of ketofol at 1mg/kg bwt in group I and bolus of fentofol at 1.5µgg/kg bwt in group II. They observed that there was statistically significant difference between the patients in two groups with respect to recovery time, as the mean recovery time was less (5.64±1.25) in ketofol group than fentofol group (6.38±1.02 mins).They mentioned that infusion rate while performing TIVA is more important for quick recovery and tapering the infusion rate towards the end of the procedure and stopping the infusion at the time of skin sutures results in very rapid recovery. They concluded that though ketofol and fentofol can be used for in TIVA infusion for elective surgeries, ketofol is safer and more efficacious.

Thejashree *et al.* (2018) conducted an experiment in twelve Beagle dogs to evaluate the propofol and ketofol following atropine, diazepam and fentanyl premedication. For the study, dogs were divided into two equal groups with six animals each. Premedication included subcutaneous administration of atropine sulphate at 0.04mg/kg b.wt., diazepam at 0.5mg/kg b.wt. and fentanyl at 0.002mg/kg b.wt. intravenously. Ketofol (1:1, 3mg/kg each in a single syringe) was given intravenously in group I and propofol was given at 6mg/kg b.wt. intravenously. They observed that recovery from anesthesia was rapid and smooth without struggling in both groups. However, it was slightly prolonged in the dogs from propofol group. They concluded that, prolonged recovery might be due to high dose of propofol compared ketofol preparation.

2.2 Clinico-physiological Parameters

These parameters were recorded before induction, after induction, during surgical procedure and at recovery

2.2.1 <u>Rectal Temperature (ºF)</u>

Amin and Atiyah (2014) evaluated the general anaesthasia induced by propofol, ketamine protocol in rabbits premedicated with diazepam. The experiment was conducted on seventeen healthy male adult local rabbits. They were premedicated with diazepam at 1mg/kg b.wt. intramuscularly. Induction was carried out with propofol at 10mg/kg b.wt. I.V.

followed by ketamine at 25mg/kg b.w. I/M. The results of the study showed that rectal temperature was decreased gradually from 0 min to 60 min. It was concluded that rectal temperature was affected by sedative effect of diazepam which led to reduction in metabolism, muscle relaxation and depression of CNS.

Kennedy and Smith (2015) conducted an experiment in ten female Beagle dogs to compare the physiological effects of total intravenous anesthesia with propofol and ketamine propofol combination at 1:1 mg/ml concentration. Anesthesia was induced with treatment drugs and then immediately after endotracheal intubation, the CRI was administered at a starting rate of 0.4 mg/ kg/ min of propofol through syringe pumps. They observed that both the anesthetic protocols resulted in slight decrease in body temperature during 60 minutes of anesthesia.

Njoku (2015) studied the physiological effects in ketamine and propofol induced dogs maintained with either repeated boluses or constant infusion of propofol. He observed that there was progressive reduction in the rectal temperature of the anesthetized animals. He concluded that the gradual decrease in the body temperature might be contributed due to shaving or clipping of larger surface area, extensive surgical incision, physiological effects of the anesthetic drug causing central nervous system depression and muscle relaxation, infusion of cold fluids, deep anesthesia, long surgical procedures and poor physical status of the patient.

Chandrakala *et al.* (2017a) studied the physiological alterations of propofol constant rate infusion in five female dogs undergoing ovariohysterectomy. All the dogs were premedicated with xylazine at 1mg/kg b.wt, atropine sulphate at 0.04mg/kg b.wt. s/c and tramadol at 3mg/kg b.wt. Anesthesia was induced with propofol ‘to effect’ until the jaw relaxation and then maintained with CRI of propofol at 0.3mg/kg/min. They observed that there was a non-significant decrease in the rectal temperature at different intervals and decreased thereafter which was found to be significant ($p<0.05$) in comparison to the baseline values. They concluded that the decrease in rectal temperature that it might be due to decrease in heat production due to decrease in muscle activity and direct effect of drugs on hypothalamus.

2.2.2 Respiratory rate (breaths/min)

Nolan and Reid (1993) performed continuous infusion of propofol in seven Beagle dogs undergoing surgery for transplanting subcutaneous tissue pouches. They observed that there was respiratory depression throughout the anesthesia however it was acceptable as the dogs were spontaneously breathing. They also observed post-induction apnea in one dog.

Correia *et al.* (1996) conducted an experiment in five Scottish blackface sheep undergoing surgery for the implantation of subcutaneous tissue pouches to investigate the pharmacokinetic effects of propofol infusion alone or with ketamine. All sheep were premedicated with Inj. acepromazine @0.05mg/kg and papaveretum @ 0.4mg/kg intramuscularly. Anesthesia was induced in Group 1 with propofol at 4mg/kg intravenously over 60 seconds and was maintained with a variable infusion rate of propofol at 0.3-0.5mg/kg/min. While in Group @ anesthesia was induced with propofol at 3mg/kg mixed together with ketamine at 1mg/kg intravenously and maintained with variable infusion rates of propofol 0.2-0.3mg/kg/min and ketamine at 0.1 to 0.2mg/kg/min separately. Infusions were administered by two volumetric infusion pumps. They observed that the respiratory rate of the sheep were well maintained throughout the infusion. Mean respiratory rate varied between 16 and 19 breaths/min during the infusion period. However, mean respiratory rate in Group 2 that is anesthesia with propofol and ketamine was higher than that in Group 1 throughout the period of anesthesia.

Nolan *et al.* (1996) performed simultaneous infusion of propofol and ketamine in ponies premedicated with detomidine to study their pharmacokinetic effects. The study was conducted on four adult ponies who were sedated with Inj. detomidine @ 20µg/kg b.wt and then anesthesia was induced with ketamine @2.2mg/kg b.wt. A bolus dose of propofol @0.5mg/kg b.wt was then administered intravenously. They observed that respiratory rates of all ponies were well maintained during the anesthesia.

Ilkiw *et al.* (2003) conducted a study in 6 cats to determine the minimum infusion rate of propofol alone and in combination with ketamine required to attenuate the reflexes commonly used in assessment of anesthetic depth in cats. For the study, all cats received three treatments with 2 weeks interval which included constant rate infusion of propofol alone, CRI of propofol combined with low-dose ketamine and CRI of propofol combined with high-dose ketamine. Anesthesia was induced with propofol till the lateral recumbency was achieved. They observed that the infusion rates used in the study were able to maintain the respiratory function even at the high doses of ketamine. They concluded that when propofol is administered in combination with ketamine it maintains the respiratory efficiency of the animals and also avoids chances of induction apnoea.

Ambros *et al.* (2008) conducted an experiment in six young adult crossbred dogs for the comparison of cardiopulmonary effects of continuous rate infusion of alphaxalone-HPCD and propofol. For the study, each dog was sedated with acepromazine (0.02mg/kg) and hydromorphone (0.05 mg/kg) intravenously. Anesthesia was induced with propofol at 4mg/kg bwt in one group and with alphaxalone-HPCD at 2mg/kg bwt. Maintenance was done with constant rate infusion of propofol at 0.25mg/kg/min and alphaxalone-HPCD at 0.07mg/kg/min for 120 mins. They observed that both drugs induced significant respiratory depression along with preanesthetics. They mentioned that respiratory depression is well-reported complication of anesthetic induction and maintenance with propofol which is believed to be caused by direct depression of the inspiratory drive and the ventilatory response to increased $PaCO_2$. The degree of respiratory depression also depends upon choice of premedication and dose and speed of administration of propofol.

Regmi *et al.* (2014) carried out an experiment in 60 human patients for the comparison of propofol-ketamine combination with propofol-butorphanol combination for TIVA on short surgical procedures. For the study, all patients were premedicated with midazolam at 2mg total dose and glycopyrrolate at 0.2 mg intravenously. They were divided into two equal group i.e. Group B and Group K. Patients from Group B were given Inj. butorphanol 20µg/kg+Inj.propofol 1.5mg/kg and Group K patients were administered with Inj. ketamine 1mg/kg + Inj. propofol 1.5mg/kg. Anaesthasia was maintained with propofol in the dose of 9mg/kg/hr through a syringe pump infusion till the end of surgical procedure. They observed that in Group K, there was statistically significant change in heart rate compared to Group B. They concluded that when propofol is combined with other anesthetic agent such as ketamine they decrease the adverse effects on respiration rate like hypoventilation, apnoea due to propofol alone. They also mentioned that ketamine or butorphanol may be combined to decrease the adverse effects of propofol alone and simultaneously decrease the amount of propofol needed.

Kennedy and Smith (2015) conducted an experiment on ten female Beagle dogs to compare the cardiopulmonary function of total intravenous anesthesia (TIVA) with propofol and 1:1 mg/ml combination of propofol and ketamine for maintenance by constant rate infusion. Anesthesia was maintained by CRI using a syringe pump at the rate of 0.4mg/kg/min by mixing 20 ml of propofol with 2ml of ketamine. The results of the study showed that treatment with admixture of ketamine- propofol resulted in more severe respiratory depression than treatment with propofol. They concluded that the negative respiratory effect of ketamine and propofol was additive in nature which caused severe respiratory depression than propofol group; however, there was no significant difference between treatments with respect to baseline cardiopulmonary values.

Njoku (2015) experimented on eight dogs to study the physiological effects of induction with ketamine and propofol and maintenance with either repeat boluses or constant infusion of propofol. He observed that the respiratory rate reduced significantly ($p<0.05$) from the baseline values in both the groups from the time of induction till recovery. He mentioned that this respiratory depression was due to complication of xylazine , propofol and ketamine which were used in the study. He concluded that, the respiratory rate of the dogs maintained with repeated boluses was significantly lower than those maintained with constant rate infusion method.

Sharma *et al.* (2016) carried out an experiment in 100 human patients undergoing short orthopedic procedures to compare the sedoanalgesic effects of TIVA infusion of ketamine-propofol (ketofol) and fentanyl – propofol (fentofol) both prepared in 1:1 combination. They observed that there were no incidences of respiratory depression in ketofol group during the study. They mentioned that the addition of low dose ketamine to propofol improves ventilation and reduces the risk of respiratory depression which is due to the effect of ketamine induced sympathoadrenal activation.

Chandrakala *et al.* (2017a) conducted an experiment in five female dogs undergoing ovariohysterectomy to study the physiological effect of constant rate infusion of propofol. All dogs were induced with propofol 'to effect' after premedication with xylazine at 1mg/kg b.wt, atropine sulphate at 0.04mg/kg b.wt s/c and tramadol at 3mg/kg b.wt. Anesthesia was maintained with CRI of propofol at 0.3mg/kg/min. They observed that respiratory rate showed a significant decrease ($p<0.05$) at 30 min as compared to baseline, however, it fluctuated non-significantly ($p>0.05$) at all intervals compared to baseline.

2.2.3 Heart rate (beats/min)

Goodchild and Serraro (1989) studied the cardiovascular effects of propofol in five beagle dogs. All the dogs were induced with alpha chloralose at 100mg/kg b.wt and maintained with infusion of propofol throughout the procedure at different dose rates for 30 min. They concluded that anesthetic doses of propofol decrease the arterial pressure and cardiac output to a greater extent.

Puttick *et al.* (1992) studied the cardiovascular effects of graded infusion rates of propofol (0.2-0.5 mg/kg/min) in dogs. The study included eight dogs of both sexes which were premedicated with morphine at 0.1mg/kg and anesthetized with bolus dose of propofol at 5 mg/kg bwt IV. The anesthesia was maintained with constant infusion of propofol at

0.2mg/kg/min. They observed that after administration of propofol, there was a reduction in the heart rate. They concluded that this marked decrease in heart rate was thought to be caused by increased vagal tone or sympatholytic effect.

Keegan and Greene (1993) studied the cardiovascular effects of a continuous two hour propofol infusion in six adult mixed breed dogs. The dogs were randomly divided into two groups and received either propofol or isoflurane as general anesthesia. Dogs from propofol group were induced @5mg/kg IV administered over 30 seconds. The infusion of propofol was started at 0.4mg/kg/min through an infusion pump. They observed that the mean values of heart rate were significantly ($p<0.05$) higher in dogs anesthetized with isoflurane compared to propofol post-induction.

Nolan and Reid (1993) carried out continuous infusion of propofol in seven Beagle dogs. They observed that during infusion, propofol causes moderate hypotension as a result of peripheral vasodilation and it contributed to the lower heart rate observed during induction and maintenance of anesthesia. They also stated that this lowered heart rate might be result of a combined effect of use of pre-anesthetic drugs as a part of sedation and propofol together.

Hellebrekers *et al.* (1998) experimented on eighty four dogs to compare the suitability of combination of medetomidine with propofol and medetomidine with ketamine. These were dogs were allotted for two groups *viz.*, propofol and ketamine group for various surgical and non-surgical procedures. All the dogs were sedated with medetomidine intramuscularly 15 minutes before induction of anesthesia. They observed that the heart rate of the dogs anesthetized with ketamine was consistently and significantly higher than that of the dogs anesthetized with propofol.

Ilkiw *et al.* (2003) conducted an experiment in cats to determine the cardiovascular effects of propofol alone and in combination with ketamine. In the study, the treatments included CRI of propofol alone, propofol combined with ketamine with high dose and low dose respectively. They observed that the cardiovascular function of the patients anesthetized with ketamine and propofol remain unchanged even at the high dose of ketamine. They concluded that when ketamine was given in combination with propofol it compensated the cardiovascular and respiratory depressant effects the propofol.

Kennedy and Smith (2015) conducted an experiment in ten female Beagle dogs to compare the cardiovascular effects of total intravenous anesthesia with propofol or 1:1 mg/ml combination of propofol and ketamine. Anesthesia was induced by IV administration of the treatment drugs to the effect at 1ml per 15 seconds of tie until intubation was complete. Maintenance was done by administration of the treatment drug by constant rate infusion using a syringe pump. They observed that treatment with propofol did not significantly affect the heart rate and treatment with ketamine-propofol resulted in significantly higher heart rate with the maximum value reaching at 10 minutes and decreasing gradually. However, there was no significant difference between treatments with respect to baseline cardiopulmonary values. They concluded that the administration of ketamine indirectly stimulated the cardiovascular system, via catecholamine release, resulting in increased heart rate.

Njoku (2015) carried out an experiment in eight adult mongrel dogs to study the physiological effects of two anesthetic protocols. They were divided in equal groups and premedicated with atropine sulphate (0.03 mg/kg bwt) and xylazine (2 mg/kg bwt). All dogs were induced with propofol at 4mg/kg bwt and ketamine at 2.5mg/kg bwt. Maintenance of anesthesia in Group I was done by repeat bolus infusion of propofol @ 2mg/kg bwt and in Group 2 with constant rate infusion of propofol at 0.2mg/kg/min. He observed that the mean heart rate of anesthetized animals reduced significantly ($p<0.05$) from the preanesthetic value. He mentioned that intermittent boluses of propofol caused significantly lower heart rate than those of dogs who were maintained with constant rate infusion technique leading to steady plasma drug concentration.

Saikia *et al.* (2016) reported the use of total intravenous anesthesia with propofol and ketamine in dogs. They stated that an appropriate selection of premedicants can improve intraoperative cardiovascular stability, perioperative analgesia and the quality of recovery. They mentioned that propofol has minimal analgesic properties and it needs to be conjugated with concurrent administration of analgesics during painful procedures. They concluded that with respect to cardiovascular parameter, a significantly higher heart rate was reported in group of dogs receiving ketamine compared to dogs receiving propofol.

Sharma *et al.* (2016) conducted an experiment in 100 human patients to compare the sedoanalgesic effects of ketamine propofol and fentanyl-propofol TIVA infusion, both prepared in 1:1 combination. All the patients were randomly and equally divided in two groups for the short orthopedic procedures of less than 30 minutes. All the patients were premedicated with injections glycopyrrolate 0.2 mg, midazolam 0.03 mg/kg IV and induced with bolus of ketofol at 1mg/kg bwt in group I and bolus of fentofol 1.5µg/kg bwt intravenously. Maintenance of anesthesia was done by the treatment drugs with continuous infusion at around 20ml/hr or more. They observed that ketamine-propofol combination produced more stable haemodynamics that fentanyl-propofol combination. They concluded that ketofol produced statistically and clinically significant increase in mean heart rate of approximately 7 beats/minute and hence is considered safe and efficacious for TIVA infusions with routine premedication.

Chandrakala *et al.* (2017a) studied the physiological effects of constant rate infusion of propofol in five female dogs undergoing ovariohysterectomy. All dogs were premedicated with xylazine at 1mg/kg, atropine sulphate at 0.04mg/kg s/c and tramadol at 3mg/kg b.wt. Dogs were induced with propofol 'to effect' and the maintained with CRI of propofol at 0.3mg/kg/min. They observed that heart rate increased marginally ($p>0.05$) at 10 and 20 min then decreased gradually, however the values were non-significant ($p>0.05$) from the baseline values up to 60 min of anesthesia. They concluded that initial increase in heart rate after premedication might be due to the effect of atropine.

Shinde *et al*. (2018) studied the clinical efficacy of ketofol and propofol as general anaesthasia in dogs. The study included total twelve dogs divided into two equal groups who underwent different surgical interventions. All dogs were premedicated with Inj. xylazine+Inj.butorphanol in a single syringe @ 2mg/kg b.wt. and 0.2mg/kg b.wt respectively and Inj.atropine sulphate @ o.o4mg/kg b.wt. Dogs from Group 1 were induced with propofol at 4mg/kg b.wt. and dogs in Group 2 were anesthetized with ketofol (1:1) @4mg/kg b.wt. intravenously. They observed that heart rate fluctuated in Group 1 after some time while it was stable in Group 2 which might be due opposing cardiopulmonary action of the individual drug producing stability throughout the anaesthasia.

Thejashree *et al.* (2017) carried out an experiment in twelve beagle dogs to evaluate the cardiovascular effects of propofol and ketofol anesthesia. They divided all the dogs in two equal groups and all dogs were premedicated with subcutaneous administration of atropine sulphate@0.04 mg/kg b.wt,, intravenous administration of diazepam @0.5mg/kg b.wt., fentanyl at 0.002mg/kg b.wt. Dogs in Group I were subjected to ketofol (1:1, each 3mg/kg b.wt.) anesthesia and in Group II propofol anesthesia was given at 6mg/kg bwt. i/v. Physiological parameters like heart rate was recorded before and at 5,10,15,30,60 and 2hrs time intervals of anesthesia. They observed that there was significant increase in heart rate after administration of anesthetics in ketofol group. They concluded that this increase might be due to cardiac stimulatory effects of ketamine.

2.3 Hematological Paramters

Schricker *et al.* (2001) carried out an experiment in twelve human patients undergoing elective colorectal surgery for the integrated analysis of glucose metabolism during surgery. For the study patients were randomly assigned to receive either TIVA with propofol and remifentanyl or sevoflurane with remifentanyl. Anesthesia in both groups was induced with

1µg/kg remifentanil given over 60 seconds followed by propofol administration at 1mg/s. Anesthesia in propofol group was maintained by constant infusion of propofol at the rate of 10mg/kg/hr and reduced to 6mg/kg/hr after 10 min. They observed that hematocrit value of propofol group decreased from 38±8 to 32±5 after 120 min of surgery.

Ilkiw and Pascoe (2003) conducted an experiment in six cats to study the haemodynamic effects of propofol and propofol-ketamine combination for TIVA. For the study, cats were anesthetized with propofol at 6.6mg/kg bwt, and then maintained with constant infusion at 0.22mg/kg/min for 60 minutes. Blood samples were taken for estimation. A noxious stimulus was applied for 5 min and again blood samples were taken. Later propofol concentration was decreased to 0.14mg/kg/min and a bolus dose of ketamine was administered at 2mg/kg and CRI was started at the rate of 23µg/kg/min and continued for further 60 min. They observed that all the hematological parameters were not affected by the addition of ketamine and reduction in dose of propofol. They concluded that administration of propofol by CRI for maintenance of anesthesia induced stable hemodynamics.

Pascoe *et al.* (2006) carried out an experiment in cats to determine the effect of propofol anesthesia on recovery. For the study total six healthy adult spayed female cats were included which underwent three different anesthetic protocols. Induction was carried out with propofol as a bolus at 5mg/kg/min till they had sluggish withdrawal response. The propofol infusion rate was started at 0.4mg/kg/min and it was continued till 30mins in T30 group and for 150 mins in T150 group. They observed that the values for packed cell volume decreased during propofol infusion. They concluded that this decrease might be due to splenic sequestration or due to changes in the peripheral circulation.

Fani *et al.* (2008) conducted an experiment in six healthy mongrel dogs undergoing major or minor surgeries to evaluate the haematological changes during epidural administration of xylazine. All the dogs were administered atropine sulphate @0.04 mg/kg i/m and xylazine HCl @0.75 mg/kg b.wt. at lumbosacral epidural space. Haematological parameters were estimated at 0 minute before the administration of drug and and then at

10, 20, 30, 60, 90 and 120 minutes. They observed a significant decrease in TEC value and non-significant decrease in TLC value.

Khameneh *et al.* (2012) evaluated clinical and paraclinical effects of intraosseous vs intravenous administration of propofol on general anesthesia in rabbits. Thirty male rabbits were divided into two experimental and three control groups each containing six. They compared induction time (sec) of two groups receiving propofol by intravenous route (group 1) and intraosseous route (group 2). They observed decrease in Hb, total erythrocyte count and PCV however it was non significant compared to the baseline value. Further they also found unaltered eosinophil, basophil and monocyte counts during the perianesthesia period, even in control groups.

Singh *et al.* (2014) conducted a hematological study in twenty four dogs for comparative evaluation of xylazine and midazolam on propofol-halothane anaesthasia. For the study, the divided the dogs in three equal groups. Dogs from Group A were given xylazine @ 0.5mg/kg b. wt., dogs from Group B were given midazolam @ 0.5mg/kg b.wt. and xylazine @0.25m/kg and midazolam at 0.25mg/kg combination was used in Group C. Anaesthasia was induced with 1% propofol to the effect. The blood samples were collected at time 0 and after 15, 30, 60 and 120 min. They observed a significant decrease in Hb, PCV and TLC values in all groups.

Anandmay *et al.* (2016) studied the haematological changes following administration of propofol in combination with buprenorphine in 10 atropinized dogs. Propofol was given to effect in the control group (group 1) whereas dogs from group 2 received buprenorphine as preanesthetic @0.015mg/kg BW before propofol to effect. Atropine sulphate was injected intramuscularly @ 0.04mg/kg BW 20 min prior to each treatment. Haematological variables viz. Hb, TEC, TLC, DLC, PCV were estimated at 5, 10, 20, 30 and 60 min of propofol administration. Haemoglobin value exhibited a significant fall at 5 min in group 1 and at 10 min in group 2 after propofol administration and showed increasing trends, returning to near baseline values. PCV showed a significant fall ($p<0.05$) at 5 min of observation in both groups, whereas, TEC exhibited a significant fall at 10min of observation in both the groups. However, the values of Hb, PCV and TEC afterwards at different intervals of observation showed increasing trends and returned near to the baseline value.

Chandrakala *et al.* (2017a) conducted an experiment in five female dogs undergoing ovariohysterectomy to study the hematological alterations after the administration of tramadol and xylazine and propofol anesthesia. All the dogs were premedicated with atropine sulphate s/c at 0.04mg/kg b.wt, xylazine at 1mg/kg b.wt and tramadol at 3mg/kg b.wt. Anesthesia was induced with propofol 'to effect' and maintained by CRI of propofol at 0.3 mg/kg/min. They observed that haemoglobin, packed cell volume, total leucocyte count and differential leucocyte count exhibited non-significant alterations ($p>0.05$) at different intervals.

Chandrakala *et al*. (2017b) conducted an experiment in ten female dogs undergoing elective ovariohysterectomy for the evaluation of haemato-biochemical changes during ketamine- butorphanol as analgesic in xylazine and propofol anaesthasia. All dogs were divided randomly in two equal groups. They were administered atropine sulphate @ 0.04mg/kg s/c. Dogs from Group I received xylazine @1mg/kg b.wt. IM and ketamine @ 3mg/kg b.wt. IM. Dogs from Group II received xylazine at 1mg/kg and butorphanol at 0.2mg/kg b.wt. IM. They observed relative neutrophilia and lymphopenia were consistent findings. Also, values of haemoglobin and PCV did not reveal any significant variation within and among the groups.

Shinde *et al.* (2018) studied the clinical efficacy of ketofol and propofol in dogs undergoing different surgical interventions. For the study total twelve dogs were selected and divided into two equal groups. All the dogs were premedicated with Inj. xylazine at 2mg/kg and Inj. butorphanol at 0.2mg/kg b.wt in a single syringe. Dogs from Group 1 were anesthetized with propofol at 4mg/kg b.wt while dogs from Group 2 were anesthetized with ketofol (1:1) at 4mg/kg b.wt. intravenously.The results of the study showed that there were fluctuations in the PCV values in Group 1 while Group 2 showed a decreasing trend in the values which were statistically non-significant. They also observed a non-significant decrease in TEC values within the intervals and between the groups within normal physiological limits. They concluded that these alterations might be due to splenic sequestrations or shifting of fluids from extravascular compartments to intravascular compartments to maintain the cardiac output during anaesthasia.

Thejashree *et al.* (2018) evaluated the propofol and ketofol anesthesia in twelve beagle dogs with respect to the hematological parameters. The clinical cases were divided into two equal groups in which were subjected to either propofol or ketofol anesthesia. All dogs were premedicated with atropine sulphate @0.04mg/kg s/c, Inj. diazepam at 0.5mg/kg and Inj. fentanyl at 0.002mg/kg intravenously. Dogs from Group I were induced and maintained with ketofol (1:1, each 3mg/kg in a single syringe) and dogs from Group II were induced and maintained with propofol anesthesia at 6 mg/kg intravenously. Hematological parameters were estimated at 0, 30, 60 min and 2 hrs interval. They observed that hematocrit values decreased significantly in both groups during post anesthetic period.

2.4 Biochemical Parameters

Kim and Jang (1999) carried out an experiment in three groups of dogs to study the effects of xylazine as preanesthetic on propofol anesthesia in three groups of dogs. They observed non significant changes in AST and ALT values. Further recorded non significant increase in BUN values in group 3 (premedicated with xylazine-2 mg/kg) after propofol anesthesia and suggested that premedication with xylazine @ 1 mg/kg BW would help to reduce the dosage of propofol and incidence of side effects.

Desborough (2000) studied the stress response of the body to trauma and surgery in terms of metabolic and endocrine activities. He mentioned that cortisol secretion from the adrenal cortex increases rapidly following the start of the surgery, as a result of stimulation by ACTH.

Schricker *et al.* (2001) conducted an experiment in twelve human patients undergoing elective colorectal surgery for the integrated analysis of glucose metabolism during surgery. For the study patients were randomly assigned to receive either TIVA with propofol and remifentanyl or sevoflurane with remifentanyl. Anesthesia in both groups was induced with 1µg/kg remifentanil given over 60 seconds followed by propofol administration at 1mg/s. Anesthesia in propofol group was maintained by constant infusion of propofol at the rate of 10mg/kg/hr and reduced to 6mg/kg/hr after 10 min. Intravenous glucose was administered at the infusion rate of 0.22µmol/kg/min. They observed that plasma concentrations of glucose increased to a comparable extent in both the groups ($p<0.05$). They concluded that decreased plasma glucose concentration indicates diminished whole body glucose tolerance. Hence, hyperglycemic response during surgical trauma is caused by impaired glucose utilization and not by stimulated gluconeogenesis.

Yasuda *et al.* (2013) carried out an experiment in rats for the evaluation of hyperglycemia due to insulin resistance because of propofol anesthesia. For the study, rats were induced with intravenous administration of propofol at 10mg/kg followed by constant infusion of 40mg/kg/hr. Blood glucose levels were determined by the glucose oxidase method. The results of the study showed that anesthesia with propofol induced a marked whole body insulin resistance and insulin stimulated glucose uptake was largely decreased in most of the muscles of the body. They concluded that propofol induced insulin resistance might affect the prognosis of the critically ill patients not only by promoting hyperglycemia, also by enhancing muscle wasting particularly due to long-term infusion.

Okwudili *et al.* (2014) studied the biochemical effects of xylazine, propofol and ketamine anaesthasia in West African dwarf goats. The study included total twenty male goats that were randomly divided into five treatment groups. Control Group were administered normal saline, group K+X (5mg/kg IV ketamine + 0.05mg/kg IV xylazine), group P + X (5mg/kg IV propofol + 0.05mg/kg IV xylazine), group P + K (propofol 5mg/kg IV + ketamine 5mg/kg IV), and group P + K + X (propofol 2.5mg/kg IV + ketamine 2.5mg/kg IV + xylazine 0.05mg/kg IV), respectively. They observed non-significant variation in serum creatinine values in all the groups while BUN value was decreased in group P+K+X. All the biochemical changes were transient. They concluded that P+K+X would be the best combination considering the biochemical parameters.

Singh *et al.* (2014) conducted a biochemical study in twenty four dogs for comparative evaluation of xylazine and midazolam on propofol-isoflurane anaesthasia. Twenty four dogs used for he study were divided in three equal groups who underwent xylazine (at 0.5mg/kg in Group A), midazolam (0.25mg/kg in Group B) and combination at 0.25mg/kg each in Group C. Induction was carried out with 1% propofol in all groups to the effect and then maintained with isoflurane. They observed an increase in plasma glucose levels in all animals which might be due increased muscular activity and sympathetic stimulation caused by restraining of animals leading to increased secretion of adrenocortical hormone.

Njoku (2015) carried out an experiment in eight dogs for investigating biochemical indices of dogs anesthetized with propofol-ketamine and maintained with either repeat bolus or constant infusion of propofol. The clinical cases were divided in two equal groups and gastrotomy was performed on all dogs. Anesthesia was induced with propofol (at 4mg/kg bwt) and ketamine (at 2.5 mg/kg bwt). Maintenance of anesthesia was done in Group 1 with repeat boluses of propofol and in Group 2 with constant infusion of propofol. He studied the changes in plasma glucose concentration as an effective tool in determining the stress response during surgery. The results of the present study showed that the plasma glucose concentration was significantly ($p<0.05$) increased at the time of recovery when compared to the pre-surgical value. He also mentioned that the drugs used in the study (atropine, xylazine, ketamine, propofol) did not obliterate the response of the dogs to pain and hence lead to increased plasma glucose levels. He concluded that route of administration of anesthetic and analgesic drugs influences the stress response with regards to the glucose concentration.

Chandrakala *et al.* (2017a) conducted an experiment in five female dogs undergoing surgery for elective ovariohysterectomy to study the biochemical alterations of propofol constant rate infusion. All the dogs were premedicated with atropine sulphate at 0.04mg/kg s/c, xylazine at 1mg/kg b.wt and tramadol at 3mg/kg. Anesthesia was induced with propofol to the effect and the maintained with constant infusion at o.3mg/kg/min. They observed that there was a variable and constant increase ($p>0.05$) in blood urea nitrogen, creatinine, ALT at different intervals after the administration of drugs. However, these changes were non-significant and within normal physiological limits. Blood glucose and AST showed significant elevation ($p<0.05$) at different levels of observation. The maximum rise in glucose level was recorded at one hour of observation. This rise in blood glucose level may be due to activation of the sympathoadrenal system releasing adrenaline which in turn mobilized glycogen from liver during anesthesia. They also mentioned that α-2 agonist have been reported to increase the blood glucose level by suppressing the insulin release and stimulating glucagon release. They concluded that CRI methods for maintenance of anesthesia in canine ovariohysterectomy produced little variation in physiology and hematobiochemical profiles.

Maeda *et al.* (2018) conducted an experiment in seven (four males, three females healthy Beagle dogs to study the effect of propofol infusion on blood glucose metabolism. All the dogs were assigned for four experimental groups and they were subjected for intravenous glucose tolerance test. All dogs were pre-medicated with 0.05mg/kg atropine sulfate subcutaneously, 0.1mg/kg midazolam intravenously. General anesthesia in Group 0.4P was induced with 1% propofol @6mg/kg IV. and then maintained with 0.4mg/kg/min of propofol infusion, while in Group 0.2P it was maintained with 0.2mg/kg/min of propofol infusion. Group S received isoflurane as general anesthesia and Group A was kept as a control. A bolus of glucose injection was administered within 30 sec and blood samples were collected for glucose analysis before and after glucose administration. They observed that blood glucose levels were increased in all three groups when compared to control group. They concluded that TIVA with propofol may induce hyperglycemia and increase the risk of perioperative complications in glucose metabolism-suppressed patients including those with diabetes and the continuous rate infusion of propofol may affect glucose metabolism in dog.

Shinde *et al*. (2018) carried out an experiment to compare the clinical efficacy of ketofol and propofol in dogs undergoing different surgical procedure. Total twelve dogs were included in the study and were divided into two equal groups. All the dogs were premedicated with Inj. xylazine at 2mg/kg and Inj. butorphanol at 0.2mg/kg b.wt. intramuscularly. Anesthesia was induced in Group 1 with propofol at 4mg/kg b.wt. whereas in Group 2 it was induced with ketofol (1:1) at 4mg/kg b.wt. intravenously. Maintenance was done by same anesthetic drugs to the effect. Biochemical estimation during the period of study revealed fluctuations I AST and ALT levels in Group 1 while in Group 2 they showed comparative decrease. BUN values were elevated in Group 1 while it decreased in Group 2. Serum creatinine values did not show alterations in both the groups.

CHAPTER III

MATERIALS AND METHODS

Recently, there have been advancements in veterinary anesthetic techniques with respect to general anesthesia to provide optimum analgesia to the surgical patient. Varieties of anesthetic protocols have been developed and being used in canine practice for the sake of reducing the pain during the surgery and improve post-operative recovery. Total intravenous anesthesia using anesthetic drugs like propofol, ketamine-diazepam, and thiopentone have proved to be efficient to produce general anesthesia in canines. Constant Rate Infusion as a part of TIVA is becoming popular due to its advantages over other techniques and hence in the present study Propofol and ketamine and propofol -admixture with opioid analgesic drug like butrophanol have been used as CRI using Fluid Bag Technique.

The present study was conducted on 12 clinical cases of dogs presented to Teaching Veterinary Clinical Complex, PGIVAS, Akola for elective ovariohysterectomy. These cases were randomly divided in two equal groups irrespective of age, breed and body weight. All dogs underwent anesthetic protocol mentioned in the table as under.

Group 'A' **(n=6)**	**Group 'B'** **(n=6)**
Induction: Inj. Propofol @4mg/kg I/V Bolus Inj. Diazepam @0.25mg/kg Slow IV	**Induction:** Inj. Ketamine-Propofol admixture (1:1) @4mg/kg I/V Bolus Inj. Diazepam @0.25mg/kg Slow IV
Maintenance: CRI **Propofol + Butorphanol** Inj. Propofol @6mg/kg/hr Inj .Butorphanol @0.3mg/kg/hr	**Maintenance: CRI** **Ketamine + Propofol +Butorphanol** Inj. Ketamine-Propofol admixture @ 6mg/kg/hr Inj. Butorphanol @0.3mg/kg/hr

3.1 Pre-operative Consideration

Twelve apparently healthy female dogs were included in the present study. They were divided into two equal groups viz., Group A and Group B. All the dogs were clinically examined prior to the elective ovariohysterectomy. Pregnant, lactating dogs were not included in the study.

Dogs selected for the study were fasted for 8-10 hours and water was withheld for 8 hours prior to operative procedure. They underwent the anesthetic protocol as assigned to the group.

3.2 Calculation of doses for CRI

1. Loading/Induction dose = dose rate (mg/kg) x Body weight/ Conc.of drug (mg/ml)

2. Constant Rate Infusion:

Step 1: Amount of drug to be added (mg) = Infusion rate (mg/kg/hr)/Flow rate (ml/kg/hr) x Fluid bottle capacity

Step 2: Amount of drug to be added (ml) = Total mgs of drug/ conc. of drug (mg/ml)

Constant Rate Infusion of a drug was maintained at 5ml/kg/hr by 'Fluid Bag Technique' using a fluid bottle of 250ml capacity (Plate 3.1) containing 0.9% Normal Saline Solution with Romsons Romo Flow Microdrip infusion set having Precision Flow Rate Controller with a setting of ml/hr for flow rate management (Plate 3.2).

Prior to addition of the calculated drug volume into the fluid bag, equal amount of normal saline was withdrawn from the fluid bag to maintain the total volume.

3.3 Anaesthetic Protocol

3.3.1 <u>Preparation of propofol CRI</u>

Propofol at the rate of 6mg/kg/hr i.e. total 30ml along with Inj. butorphanol at 0.3mg/kg/hr i.e. total 7.5ml was added in the normal saline bag in group A (Plate 3.3).

Plate 3.1 Normal saline (0.9%) bag of 250 ml capacity

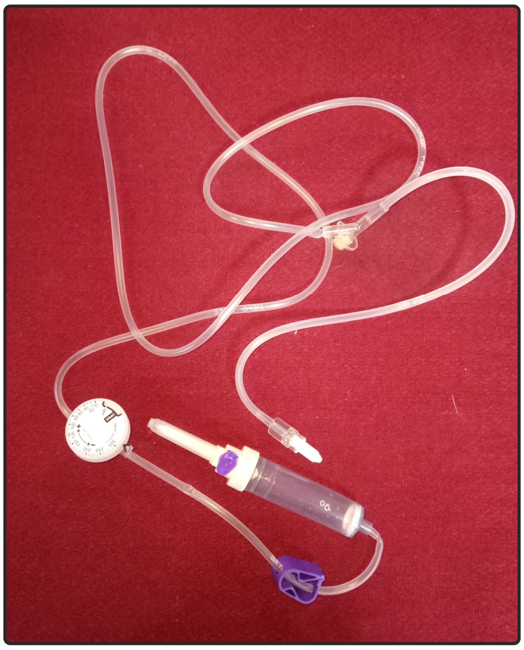


Plate 3.2 Romson's Microdrip Infusion Set with precision flow-rate controller

Plate 3.3 Anesthetic solution for CRI

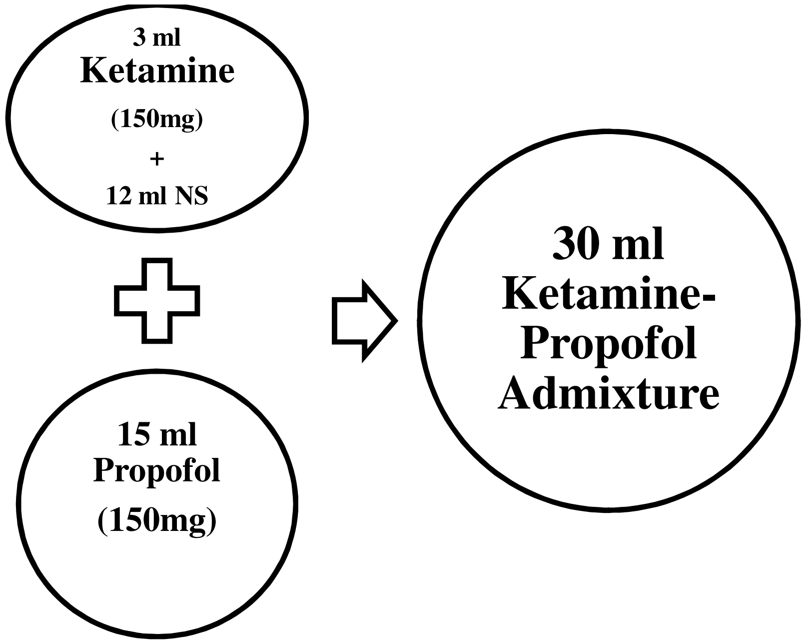
a) Ketamine

b) Propofol

c) Butorphanol

Plate 3.4 Anaesthetic drugs used in the study

3.3.2 Preparation of Ketamine-Propofol Admixture (1:1) CRI



In this study, commercially available anesthetic drugs like (Inj. ketamine (Aneket) - 50 mg/ml, Inj. propofol (Neorof) 10 mg/ml and Inj. butorphanol (Butodol) – 2 mg/ml were used (Plate 3.4)

In order to prepare the ketamine-propofol admixture at 1:1 ratio for 30ml volume, three ml of ketamine (150 mg) was mixed in 12 ml of normal saline to make 15 ml of mixture, each ml containing 10mg of ketamine and 15 ml of propofol (10 mg/ml i.e. 150 mg) was mixed with ketamine mixture (10mg/ml) in a normal saline (0.9%) bag of 250ml capacity. Each ml of this admixture contains 5 mg of ketamine and 5 mg of propofol. Inj. butorphanol at the rate of 0.3 mg/kg/hr i.e. 7.5 ml as a part of CRI technique was added in the normal saline bag separately along with ketamine-propofol admixture in group B.

3.4 Preparation of Animal

All dogs in the study irrespective of the group were sedated with Inj. xylazine @ 2 mg/kg body wt. intramuscularly.

After sedation, the ventral midline site caudal to umbilicus was prepared aseptically by clipping, shaving and scrubbed by using povidone iodine (7.5%) cleansing solution. Cephalic vein was cannulated (Plate 3.5). Induction was undertaken (Plate 3.6) as per the anaesthetic protocol assigned for respective group and constant rate infusion was started immediately after induction by using Romsons Romo Flow Microdrip infusion set having Precision Flow Rate Controller. Patient was positioned in dorsal recumbency (Plate 3.7). Surgical site was draped to avoid contamination of the surgical site (Plate 3.8).

3.5 Pre-anesthetic Medication

All the dogs in the study were pre-medicated as follows :

Inj. meloxicam 0.3 mg/kg body weight IM

Inj. amoxicilin @10 mg/kg body weight IM

Inj. chlorpheniramine maleate @ 0.5 mg/kg body weight IM

3.6 Induction

Dogs from Group A were induced with Inj. propofol @4mg/kg Body weight and Inj. diazepam @0.25 mg/kg Body weight slow intravenously

Dogs from Group B were induced with Inj. ketamine-propofol admixture @4 mg/kg Body weight and Inj. diazepam @0.25 mg/kg body weight slow intravenously.

Plate 3.5 Cannulation of Cephalic vein

Plate 3.6 Induction of anaesthesia by intravenous bolus administration

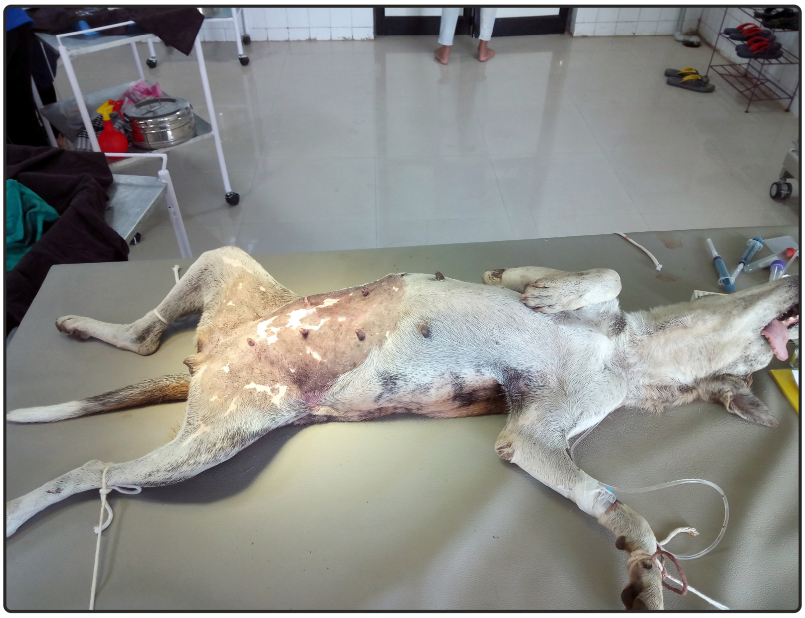


Plate 3.7 Positioning of patient in dorsal recumbency

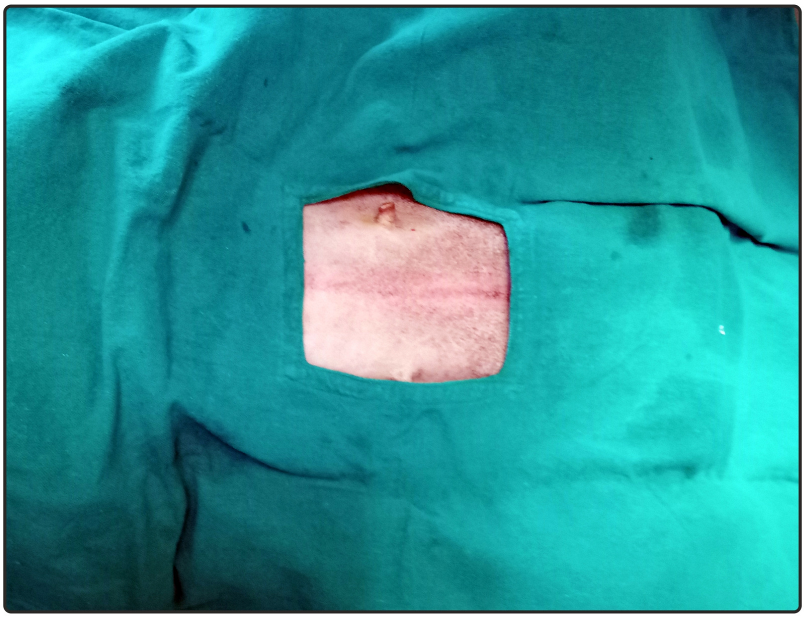


Plate 3.8 Draping the surgical site

3.7 Endotracheal intubation

All surgical patients were intubated using appropriate size of ET tubes after induction of anesthesia to combat respiratory emergency likely to occur during anaesthetic period.

3.8 Maintenance of Anaesthesia

Dogs from Group A were maintained with constant infusion of Inj. propofol at 6 mg/kg/hr and Inj. butorphanol @0.3 mg/kg/hr however, dogs from Group B were maintained with constant infusion of ketamine-propofol admixture at 6 mg/kg/hr and Inj. butorphanol @0.3 mg/kg/hr added to a normal saline bag of 250ml capacity respectively through a microdrip infusion set (Plate 3.9).

3.9 Surgical Technique

Ovariohysterectomy procedure was performed as per the standard procedure described by Fossum *et al.* (2013).

In the present study ovariohysterectomy was performed by double-clamp method. After identifying the umbilicus, an incision was taken along the ventral midline about 1cm caudal to the umbilicus (Plate 3.10). An incision of about 3-4 cm was made through skin and subcutaneous tissue to expose linea alba. Linea alba was grasped, tented outwards and a stab incision was made into abdominal cavity. Linea alba was extended cranially and caudally to the stab with scissors. Left abdominal wall was elevated by grasping the linea alba and ovariectomy hook was slided inside against the wall, 2 to 3 cm caudal to the kidney. The hook was then turned medially ensnaring the uterine horn and broad ligament. Identification was confirmed by following it to either the uterine bifurcation or ovary. Suspensory ligament was stretched by using the index figure by applying the caudolateral traction without tearing the ovarian vessels to allow the exteriorization of the ovary. A hole was made in the broad ligament caudal to ovarian pedicle and two artery forceps were placed proximal to the ovarian pedicle (Plate 3.11). While using two clamp method, the ovarian pedicle clamps served both to hold the pedicle and make a groove for ligature. A figure-eight ligature using Chromic catgut no. 0 was placed. The clamp was removed and ligature was tightened to allow pedicle compression. Ovarian pedicle was transected and was checked for hemorrhages. After tracing the contra-lateral ovary, same procedure was followed.

A window was made into broad ligament adjacent to the uterine body, uterine artery and vein. Ligature was applied if the patient was in estrus or if the broad ligament was heavily infiltrated with vessels or fat. After placing the artery forceps across the broad ligament, it was transected.

The uterine body was exposed (Plate 3.12) and ligated cranial to the cervix by placing a figure-eight suture encircling the uterine vessels. The uterine body was transected and checked for hemorrhages . Uterine stump was replaced in the abdominal cavity. Abdominal wall was closed in three layers. Peritoneum and linea alba were sutured by placing continuous lock-stitch sutures and subcutaneous tissue was sutured by placing continuous sutures using Vicryl no. 1. Skin was apposed by placing intradermal sutures (Plate 3.13).

3.10 Parameters studied

The various clinico-physiological, hematological and biochemical parameters were recorded before induction, after induction, during anaesthesia (at 30 min) and at recovery. The following observations were recorded in all the animals under study.

3.10.1 Clinical parameters

(a) Assessment of anesthesia

i) Quality of anaesthasia

The quality of anaesthesia was judged by observing various reflexes exhibited by the patient during the surgical procedure.

Plate 3.9 Maintenance of anaesthasia on CRI

Plate 3.10 Ventral midline incision

Plate 3.11 Ligation of ovarian pedicle by double clamp method

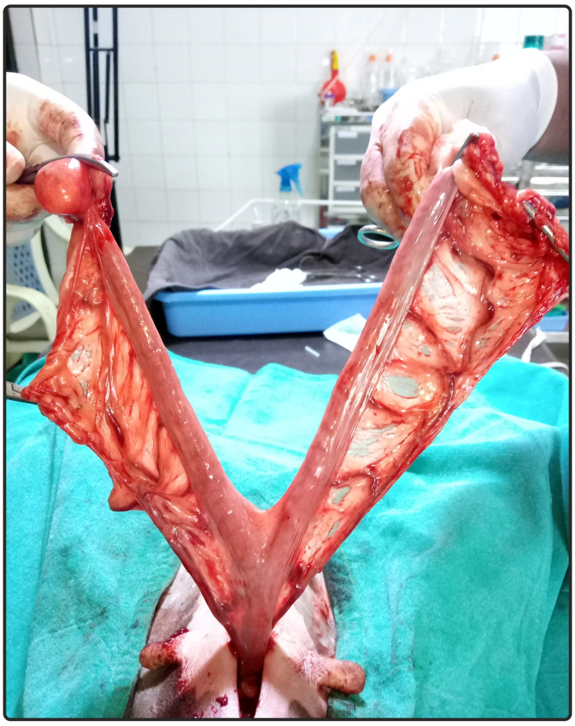


Plate 3.12 Exteriorizing the uterine pedicle

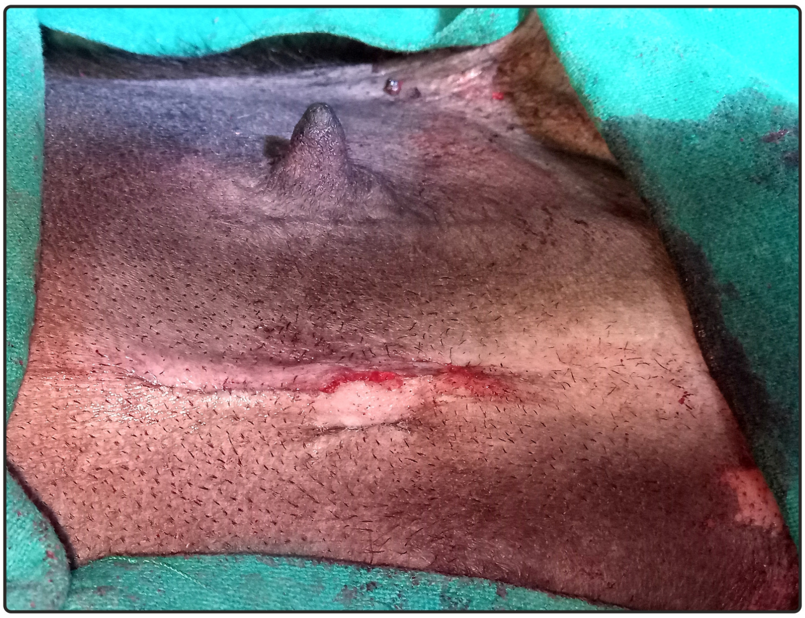


Plate 3.13 Closure of surgical wound

1. Palpebral Reflex

Palpebral reflexes were checked in terms of absent or present to decide the quality of anesthesia.

2. Jaw tone

Jaw tone was evaluated as relaxed or present during the infusion of anesthetic drug (Plate 3.14).

3. Eyeball position

Position of eyeball during the surgical procedure was checked to ensure that the patient is in deep anesthesia. Mid-ventral or ventral placement of eyeball is desirable during the procedure in case of propofol anesthesia (Plate 3.15).

4. Pain response on surgical stimulus

During the procedure, any pain response exhibited by the patient upon surgical stimulus was observed and accordingly necessary steps were taken to combat the problem.

(b) Recovery (In Minutes)

Recovery time was recorded as time interval (in minutes) between the cessation of infusion of anesthetic drug and the dog's ability to lift the head.

3.10.2 <u>Physiological parameters</u>

All the physiological parameters were recorded before induction, after induction, during the surgical procedure (at 30 min) and at recovery. The following physiological parameters were recorded-

(a) Rectal temperature (°F)

The rectal temperature was measured in °F before induction, after induction of anesthesia, during the surgical procedure and at recovery.

(b) Respiratory rate (breaths/min)

The respiratory rate (breaths/minutes) was recorded before induction, after induction of anesthesia, during the surgical procedure and at recovery.

(c) Heart rate (beats/min)

The heart rate (beats/minutes) was recorded before induction, after induction of anesthesia, during the surgical procedure and at recovery (Plate 3.16).

3.10.3 Haematological parameters

All blood samples were processed immediately after collection on Abaxis automatic hematological analyzer.

Blood samples were collected from cephalic vein after sedation, during surgical procedure at 30 min of starting of procedure and at recovery for the evaluation of hematological parameters (Plate 3.17).

(a) Haemoglobin (g/dL)

Hemogloblin was estimated by automatic haemo-analyzer by Abaxis and the values were expressed in grams per deciliter (Plate 3.18).

(b) Packed cell volume (%)

Packed cell volume was estimated by using automatic haemo-analyzer by Abaxis The values were expressed in percentage.

(c) Total erythrocyte count (cells$\times 10^6$/cu.mm)

Total erythrocyte count was estimated by automatic haemo-analyzer by Abaxis.The values were expressed in 10^6 per cubic millimeter.

(d) Total leucocyte count (cells$\times 10^3$/ cu.mm)

Total leucocyte count was estimated by automatic haemo-analyzer by Abaxis. The values were expressed in 10^3 per cubic millimeter.

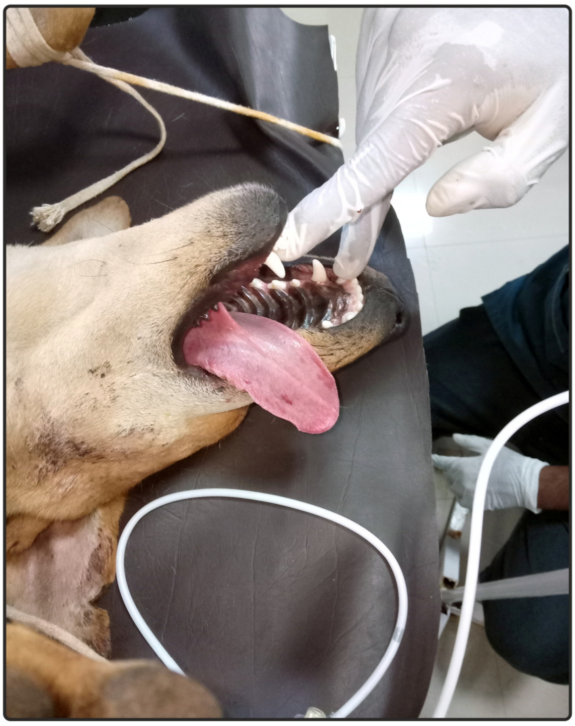


Plate 3.14 Monitoring of patient (Jaw tone reflex)

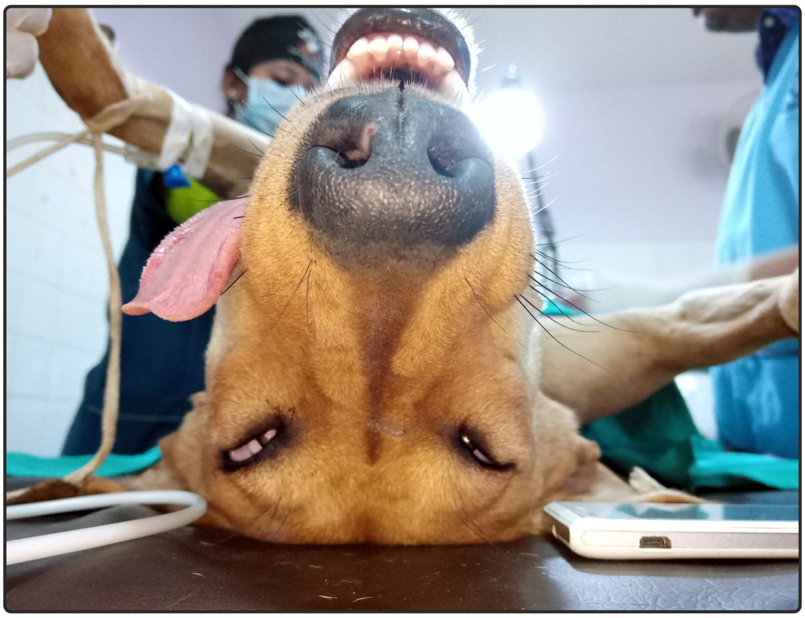


Plate 3.15 Mid-Ventral position of eyeball

Plate 3.16 Monitoring the patient after induction

Plate 3.17 Collection of blood sample post-operatively

(e) Differential Leukocyte Count (DLC) (%)

Differential Leucocyte Count (DLC) was carried out with automatic haemo-analyzer by Abaxis. The individual cell counts were expressed in percentage.

3.10.4 Biochemical parameters

All the following biochemical parameters were estimated by using Vetscan semi-automatic biochemical analyzer (Plate 3.19).

Serum was separated after half an hour from clot activator and then it was transferred into appendorph tubes and centrifuged at 3000 rpm for 5 minutes for biochemical evaluation.

(a) Alanine aminotransferase ALT (IU/L)

Estimation of alanine aminotransferase was carried out by using AGD diagnostics kit and the values were expressed in IU/L.

(b) Aspartate aminotransferase AST (IU/L)

Estimation of aspartate aminotransferase was carried out by using AGD diagnostics kit and the values were expressed in IU/L.

(c) Serum creatinine (mg/dL)

The serum creatinine was estimated by using AGD diagnostics kit and the values were expressed in mg/dL.

(d) Blood urea nitrogen (BUN) (mg/dL)

The Blood urea nitrogen values were estimated by using AGD diagnostic kit and the values were expressed in mg/dL.

(e) Blood glucose (mg/dL)

Blood glucose was estimated by using AGD diagnostic kit and the values were expressed in mg/dL.

3.11 Statistical Analysis

The data recorded during the study was statistically analyzed by Analysis of Variance using WASP 2.0 with Two Factor Factorial Experiment.

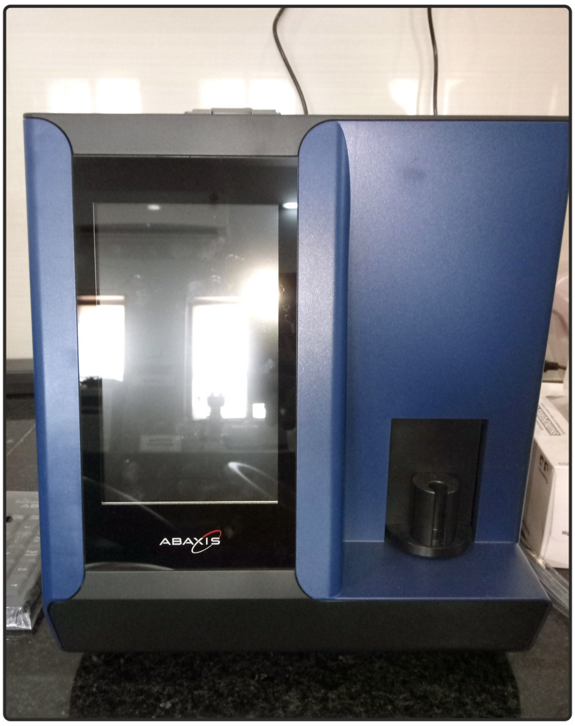


Plate 3.18 Abaxis automatic haematological analyzer

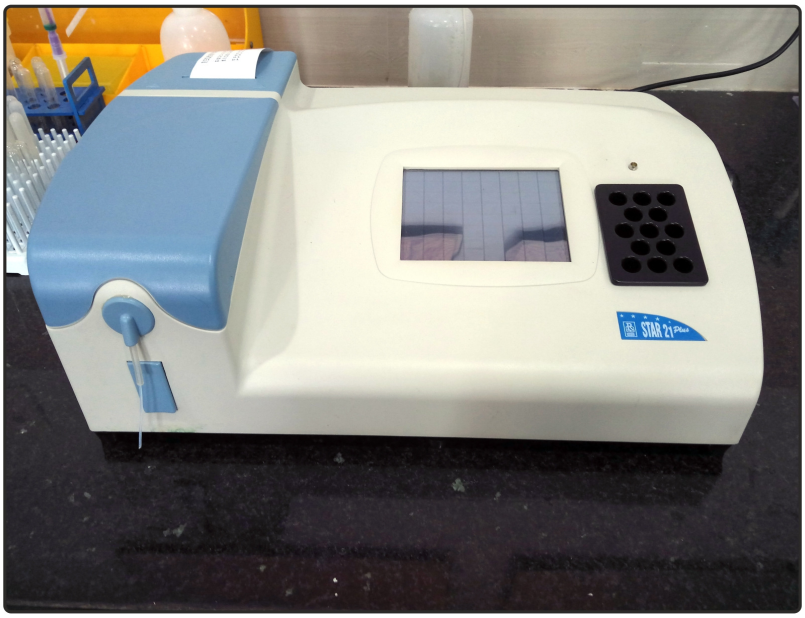


Plate 3.19 Vetscan semi-automatic biochemical analyzer

CHAPTER IV

RESULTS AND DISCUSSION

The present study entitled "Anaesthetic Efficacy of propofol and ketamine-propofol admixture with butorphanol as Constant Rate Infusion using Fluid Bag Technique in Dog" was carried out in 12 clinical cases of dogs presented to Teaching Veterinary Clinical Complex, Akola for elective ovariohysterectomy. These cases were randomly divided into two equal groups viz., Group A and Group B.

For the evaluation of anesthetic efficacy of the two treatment protocols, several parameters were evaluated before and during the period of anesthesia which includes quality of anesthesia, hemato-biochemical estimations at different intervals of time.

All the surgical patients were sedated with Inj. xylazine @2mg/kg b.wt intramuscularly. Premedication was given in the form of prophylactic antibiotic i.e. Inj. amoxicilin+ cloxacilin @10mg/kg b.wt, Inj. meloxicam @0.3mg/kg b.wt as an anti-inflammatory agent and Inj. chlorpheniramine maleate @0.5 mg/kg b.wt as an antihistaminic agent intramuscularly.

Dogs from Group A were induced Inj. propofol @4 mg/kg b.wt. and Inj. diazepam @0.25 mg/kg b.wt. intravenously. Maintenance of anesthesia was carried out by constant infusion of Inj. propofol at 6mg/kg/hr and Inj. butorphanol @0.3mg/kg/hr through microdrip infusion set added to normal saline bag of 250 ml capacity. Similarly dogs from Group B were induced with ketamine and propofol admixture (1:1, each 5mg/ml) at 4mg/kg b.wt. intravenously and maintained with the constant infusion of the same admixture at 6mg/kg/hr and Inj. butorphanol @0.3 mg/kg/hr. Flow rate in both the groups were maintained at 5 ml/kg/hr.

The average values of various parameters estimated during the research work are presented and discussed as under.

4.1 Assessment of anesthesia

To judge the anesthetic efficacy of two anesthetic protocols, assessment of anesthesia was carried out during and after the procedure which includes recording of reflexes exhibited by the dog during the anesthetic procedure if any and time required for recovery.

4.1.1 Quality of anesthesia

The quality of anaesthasia in both the groups was assessed by judging the various reflexes such as pedal reflex, eye ball position, jaw-tone and palpebral reflex.

In Group A induction apnoea was observed in all the patients. The reflexes were abolished after the induction and the patients were in surgical plane of anaesthasia throughout the procedure. Eye balls were placed mid-ventrally and jaw-tone was relaxed. No patient showed any reflex upon painful stimulus.

In Group B, smooth induction of anesthesia without apnoea was observed as compared to Group A. Corneal and palpebral reflexes were not abolished completely in all patients (Amin and Atiyah, 2014). Eyeballs were placed mid-ventrally in all the patients.

4.1.2 Recovery time

Recovery time is defined as the period between the end of infusion till lifting of head.

The mean values observed in both the groups have been tabulated in Table 4.1. and elaborated graphically in Fig. 4.1. One Way ANOVA analysis of the same has been presented in Table 4.2.

Table 4.1 Mean ± SE value of recovery time for both the groups expressed in min

Group	Average Recovery Time (min)
Group A	22.67 ± 1.28
Group B	15.33 ± 1.71

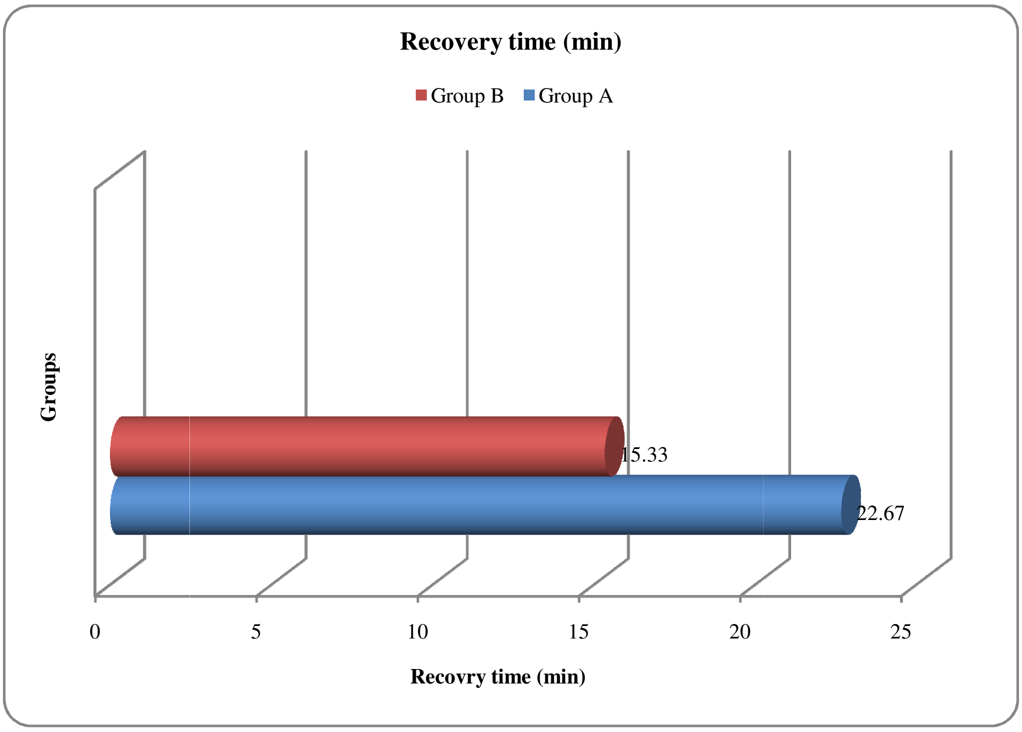


Fig. 4.1 Histogram showing mean value of Recovery time (min) of both the groups

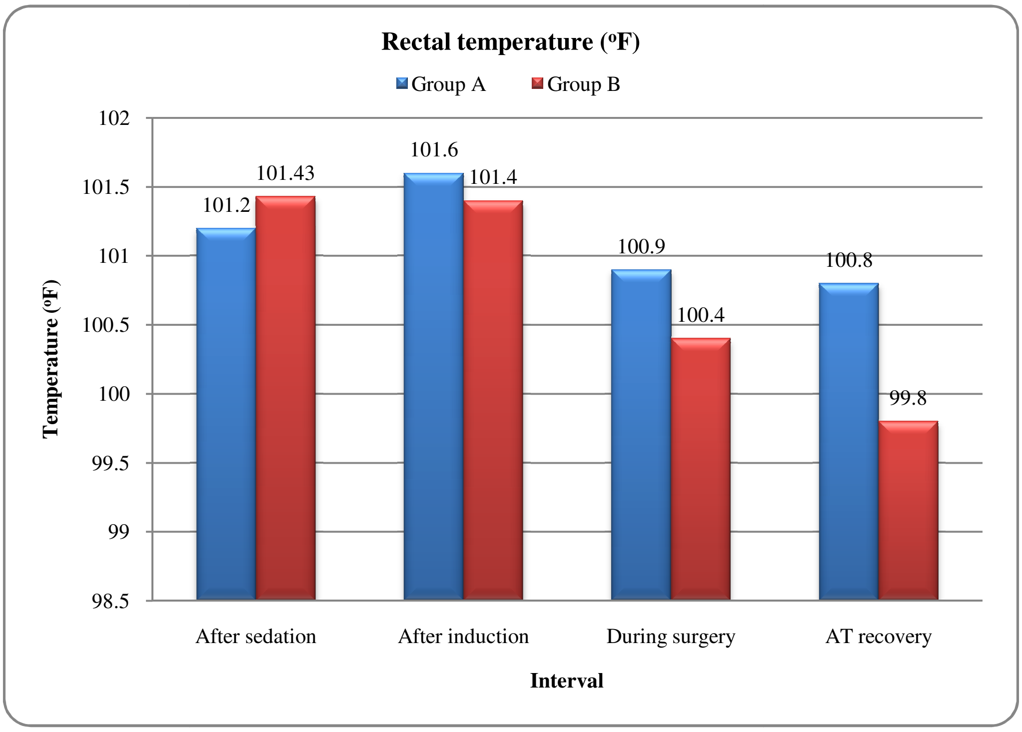


Fig. 4.2 Histogram showing the mean values of Rectal temperature (^{o}F) in both the groups

Table 4.2 Two sample t Test for recovery time

Two Sample t Test results for Recovery time	
T – Statistic	3.436
T - Table (0.05)	2.228
T - Table (0.01)	3.169

In Group A the mean time required for recovery was 22.67 ± 1.28 while in Group B it was 15.33 ± 1.71 minutes. Recovery from anesthesia was excitement and pain free without struggling in both the groups, although in Group A it was slightly prolonged (Thejashree *et al.*, 2018). Longer recovery time in Group A might be due to higher doses of propofol for short duration or lower doses for longer duration which may prolong the recovery in propofol anesthesia. Longer recovery times might also be due to the effect of diazepam which is a sedative, hypnotic (Amin and Atiyeh, 2014)

These observations made in the study are in agreement with Morgan *et al.* (1990), Nolan and Reid (1993), Nolan *et al.* (1996), Tsai *et al.* (2007), Amin and Atiyeh (2014), Njoku (2015) and Thejashree *et al.* (2018).

4.2 Clinico-physiological parameters

In the present study, clinico-physiological parameters were recorded before induction, after induction, during surgery (at 30 min) and at recovery in terms of heart rate (beats /min), respiration rate (breaths/min) and rectal temperature (degree Fahrenheit)

4.2.1 Rectal temperature (^{0}F)

Average values for rectal temperature for both the groups at different intervals are presented in Table 4.3 followed by their ANOVA values in Table 4.4 and illustrated graphically in Fig. 4.2.

Table 4.3 Mean ± SE values of rectal temperature of both groups expressed in degrees of Fahrenheit

Interval / Group	Before induction	After induction	During surgery	After recovery	Pooled mean
Group A	101.20 ± 0.26	101.60 ± 0.32	100.90 ± 0.13	100.80 ± 0.25	101.10 ± 0.17 ^{B}
Group B	101.40 ± 0.29	101.40 ± 0.28	100.40 ± 0.35	99.80 ± 0.28	100.70 ± 0.40 ^{A}
Pooled mean	101.30 ± 0.19 ^{II}	101.50 ± 0.20 ^{II}	100.60 ± 0.19 ^{I}	100.30 ± 0.24 ^{I}	

Means bearing same superscripts differ significantly.

Table 4.4 ANOVA table for Rectal temperature

Source of variation	Degrees of freedom	Sum of squares	Mean sum of squares	F cal	P value
Replication	5	3.369	0.674	1.568	
Group	1	1.802	1.802	4.193^{*}	0.048
Interval	3	11.004	3.668	8.536^{**}	0.000
Group x Interval	3	2.681	0.894	2.079^{NS}	0.121
Error	**35**	15.040	0.430	-	

*- 5% significance, ** - 1% significance, NS- Non-significant

Critical Difference Values		
-	CD 5%	CD 1%
Factor A	0.384	0.515
Factor B	0.543	0.729
Treatments/(AxB)	0.768	1.031

The normal range of rectal temperature in dogs is 99.5 to 102.5^0F (Amalendu, 2014).

In Group A, the average values of rectal temperature before induction, after induction, during surgery and after recovery was 101.20 ± 0.26, 101.60 ± 0.32, 100.90 ± 0.13 and 100.80 ± 0.17 respectively with the overall mean value of 101.10 ± 0.17. While in Group B, it was observed 101.43 ± 0.29, 101.40 ± 28, 100.40 ± 0.35 and 99.80 ± 0.28 respectively with the pooled mean 100.70 ±0.40. The overall mean values differed significantly ($p<0.05$) between the groups. In the present study, as the infusion was carried out for very short time, it did not cause any clinically significant decrease.

In both the groups, the mean rectal temperature value showed decreasing trend throughout the anaesthasia with pooled mean after induction sedation 101.30 ± 0.19 to 100.30 ± 0.24 after recovery which was statistically significant ($p<0.01$) but was within normal physiological limit and had no clinical significance.

The decrease in rectal temperature observed in both the groups during the period of anaesthasia might be due hypothermia which is produced by sedatives and anesthetics due to depression of thermoregulatory centre, reduced basal metabolic rate and muscle activity, depression of peripheral circulation and vasodilation (Njoku, 2015).

These observations recorded during the study corroborate with Amin and Atiyah (2014), Kennedy and Smith (2015), Njoku (2015) and Chandrakala *et al.* (2017a) who also observed the significant decrease in rectal temperature during propofol anaesthasia.

4.2.2 Respiratory rate (Breaths/min)

The mean values of respiratory rate observed in both groups have been tabulated in Table 4.5 and depicted in Fig. 4.3. ANOVA of the same has been illustrated in Table 4.6.

Table 4.5 Mean ± SE values of respiratory rate of both groups expressed in breaths per minute

Group \ Interval	Before induction	After induction	During surgery	After recovery	Pooled mean
Group A	16.67 ± 3.49	15.67 ± 3.80	18.33 ± 2.80	25.50 ± 5.49	19.04 ± 2.22
Group B	13.00 ±3.01	14.50 ±1.71	17.17 ±2.02	21.83 ±2.66	16.63 ± 1.94
Pooled mean	14.83 ± 2.27 ^{I}	15.08 ± 1.99 ^{I}	17.75 ± 1.66 ^{I}	23.67 ± 2.96 ^{II}	

Means bearing different superscripts differ significantly.

Table 4.6 ANOVA table for respiratory rate

Source of variation	Degrees of freedom	Sum of squares	Mean sum of squares	F cal	P value
Replication	5	714.417	142.883	2.607	
Group	1	70.083	70.083	1.279^{NS}	0.266
Interval	3	607.167	202.389	3.693^{*}	0.021
Group x Interval	3	18.750	6.250	0.114^{NS}	0.951
Error	35	1918.250	54.807	-	

*- 5% significance, NS- Non-significant

Critical Difference Values		
-	CD 5%	CD 1%
Factor A	4.338	5.822
Factor B	6.135	8.233
Treatments/(AxB)	8.677	11.643

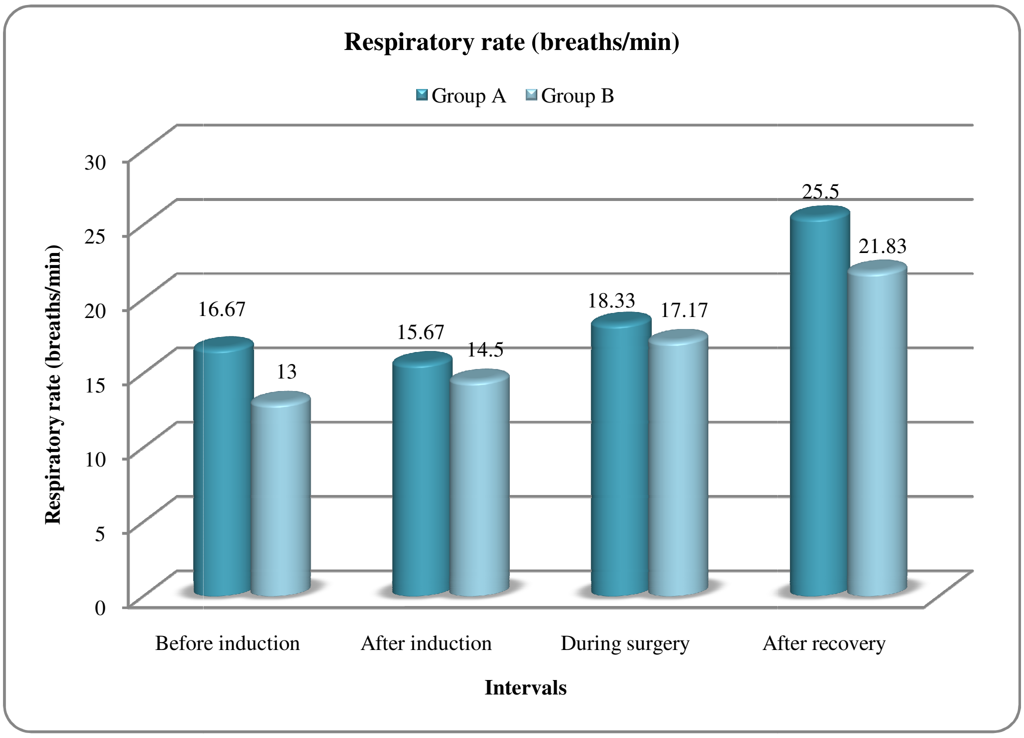


Fig. 4.3 Histogram showing mean values of the respiratory rate (breaths/ minute) in both the groups

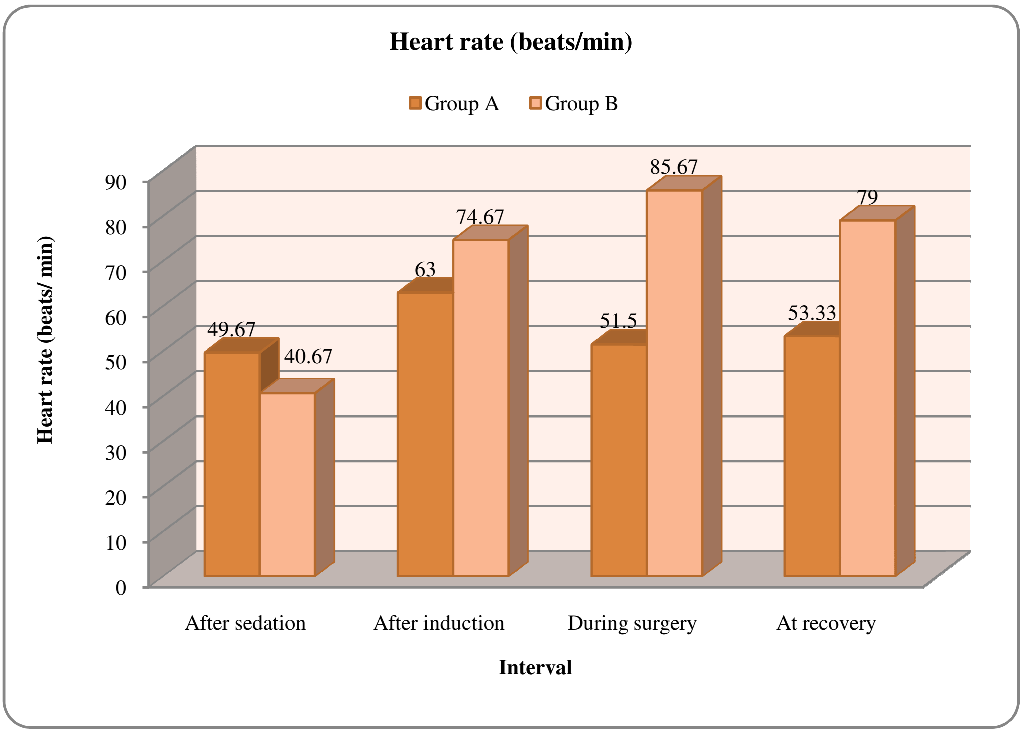


Fig. 4.4 Histogram showing the mean values of the Heart rate (beats/ min) in both the groups

The normal range of respiratory rate in dogs is 14 to 30 breaths per minute (Amalendu, 2014).

In the present study, average respiration rate in Group A before induction, after induction, during surgery and after recovery was observed to be 16.67 ± 3.49, 15.67 ± 3.80, 18.33 ± 2.80 and 25.50 ± 5.49 respectively with the pooled mean of 19.04 ± 2.22. In Group B it was 13.00 ± 3.01, 14.50 ± 1.71, 17.17 ± 2.02 and 21.83 ± 2.66 throughout the period of anaesthasia with the pooled mean of 16.63 ± 1.94. The pooled mean value for Group A was 19.04 ± 2.22 and for Group B was 16.63±1.94 which was lesser than that of Group A.

It can be observed that, respiratory rate increased after induction in Group B (14.50 ± 1.71) than baseline values which might be due respiratory stimulant action of ketamine.

The respiratory rate varied significantly ($p<0.05$) between intervals. The pooled mean value for both the groups before induction was 14.83 ± 2.27 which increased to 23.67 ± 2.96 after recovery.

The values depict that respiratory rate in Group A was stable and within limits under propofol anesthesia. Constant rate infusion of propofol for a short period of time did not cause respiratory depression and hence suffice the purpose of avoiding peaks and troughs in respiration during anesthesia. While in Group B respiratory stimulant effects of ketamine compensated the negative effects of propofol on respiration.

These findings corroborate with Correia *et al.* (1996), Nolan *et al.* (1996), Ilkiw *et al.* (2003), Kennedy and Smith (2015), Njoku (2015) and Sharma *et al*. (2016)

4.2.3 <u>Heart rate (Beats/min)</u>

The mean values of heart rate observed in both groups have been tabulated in Table 4.7 and illustrated in Fig. 4.4. ANOVA of the same has been illustrated in Table 4.8.

Table 4.7 Mean ± SE values of heart rate of both groups expressed in beats per minute

Interval / Group	Before induction	After induction	During surgery	After recovery	Pooled mean
Group A	49.67 ± 6.84	63.00 ± 7.21	51.50 ± 4.87	53.33 ± 5.55	54.38^{A} ±2.97
Group B	40.67 ± 3.22	74.67 ± 13.62	85.67 ± 20.86	79.00 ± 15.47	70.00^{B} ±10.04
Pooled mean	45.17 ± 3.85	68.83 ± 7.56	68.58 ± 11.44	66.17 ± 8.74	

Means bearing different superscripts differ significantly.

Table 4.8 ANOVA table for heart rate

Source of variation	Degrees of freedom	Sum of squares	Mean sum of squares	F cal	P value
Replication	5	6610.188	1322.038	1.920	0.116
Group	1	2929.688	2929.688	4.255^{*}	0.047
Interval	3	4687.396	1562.465	2.269^{NS}	0.098
Group x Interval	3	3200.063	1066.688	1.549^{NS}	0.219
Error	35	24097.979	688.514	-	-

*- 5% significance, ** - 1% significance, NS- Non-significant

Critical Difference Values		
-	CD 5%	CD 1%
Factor A	15.377	20.633
Factor B	21.746	29.180
Treatments/(AxB)	30.753	41.267

The normal range of heart rate in dogs is 70 to 120 beats per minute (Amalendu, 2014).

The average value of heart rate in Group A ranged from 49.67 ± 6.84 to 53.33 ± 5.55 with the pooled mean value of 54.38 ±2.97 while in Group B it varied from 40.67 ± 3.22 to 79.00 ± 15.47 with pooled mean of 70.00 ±10.04. There was significant difference ($p<0.05$) in heart rate between Group A and Group B, however the values were within normal physiological range. Comparatively lower heart rate in Group A was observed than Group B which shows that this decrease in heart rate might be due to sympatholytic effect of propofol or increased vagal tone or the combination of effect of preanesthetics i.e. xylazine and diazepam along with propofol anesthesia.

The heart rate in Group B was stable and above the values after induction due to cardiostimulant effect of ketamine.

It is observed that, in both the groups pooled mean value of heart rate before induction was 45.17 ±3.85 which showed increasing trend throughout the anaesthasia up to 66.17 ± 8.74 till recovery. Heart rate was stable in both the groups and varied non-significantly within intervals.

These observations recorded during the study are in agreement with Puttick *et al.* (1992), Keegan and Greene (1993), Nolan and Reid (1993), Hellbrekers *et al.* (1998), Ilkiw *et al.* (2003), Kennedy and Smith (2015), Njoku (2015), Sharma *et al.* (2016) and Thejashree *et al.* (2018).

4.3 Hematological estimation (g/dL)

In the present study, hematological estimation was carried out after induction, during surgical procedure (at 30 min) and at recovery.

4.3.1 Haemoglobin

The mean values for heamoglobin estimated during the study are tabulated in Table 4.9 and depicted in Fig. 4.5. ANOVA for the same has been presented in Table 4.10.

Table 4.9 Mean ± SE values for haemoglobin of both groups expressed in g/dL

Interval / Group	Before induction	During surgery	After recovery	Pooled mean
Group A	14.25 ± 0.91	14.23 ± 0.87	13.52 ± 0.90	14.00 ± 0.24
Group B	15.43 ± 0.91	15.53 ± 0.67	13.85 ± 0.73	14.94 ± 0.55
Pooled mean	14.84 ± 0.64	14.88 ± 0.56	13.68 ± 0.56	

Means bearing different superscripts differ significantly.

Table 4.10 ANOVA table for haemoglobin

Source of variation	Degrees of freedom	Sum of squares	Mean sum of squares	F cal	P value
Replications	5	70.218	14.044	6.274	0.001
Group	1	7.934	7.934	3.544^{NS}	0.071
Interval	2	11.134	5.567	2.487^{NS}	0.103
Group x Interval	2	1.671	0.835	0.373^{NS}	0.692
Error	25	55.960	2.238	-	-

NS- non- significant

Critical Difference Values		
-	CD 5%	CD 1%
Factor A	1.027	1.390
Factor B	1.258	1.702
Treatments/(AxB)	1.779	2.407

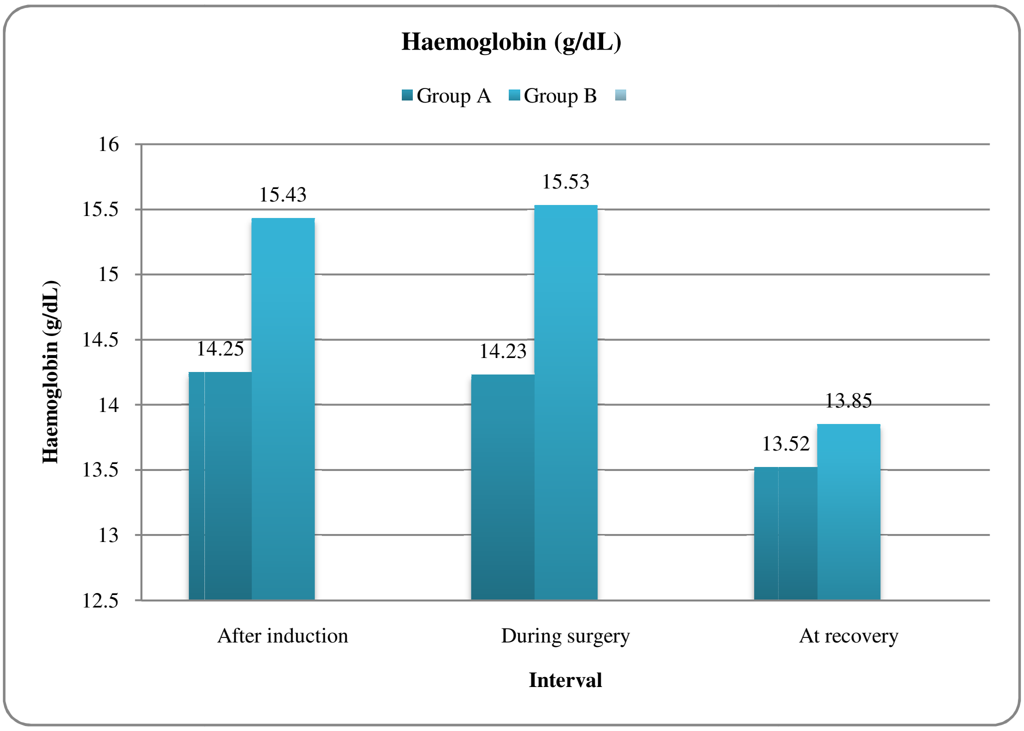


Fig. 4.5 Histogram showing mean values of the Haemoglobin (g/dL) in both the groups

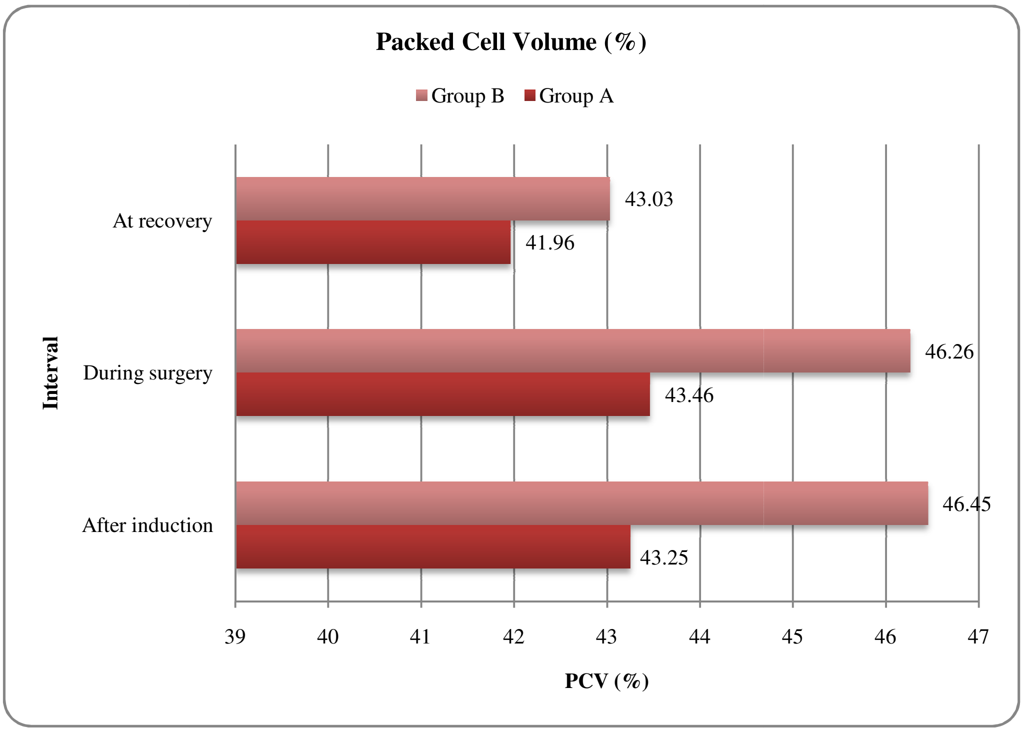


Fig. 4.6 Histogram showing the mean values of Packed cell volume (%) in both the groups

The normal range for haemoglobin in dogs is 10 to 16 g/dL (Brar *et al.,* 2014).

The average value of haemoglobin for Group A immediately before induction , during surgical procedure and after recovery was 14.25 ± 0.91, 14.23 ± 0.87 and 13.52 ± 0.90 respectively with the pooled mean of 14.00 ± 0.24. The values showed decreasing trend throughout the anesthesia in Group A which was statistically and clinically non-significant and within normal range.

In Group B, mean value before induction was 15.43 ± 0.91 which showed marginal increase during surgery to 15.53 ± 0.67 and then decreased at the end of anesthesia to 13.85 ± 0.73 with the it was within normal limit and statistically non-significant.

The pooled mean value of haemoglobin of both the groups before induction was 14.84 ±0.64 which decreased towards recovery to 13.68 ± 0.56. Although the value decreased at the end of anaesthasia in both the groups, it was clinically and statistically non-significant.

This non-significant decrease in value at recovery might be due to splenic dilation resulting in splenic sequestration of RBCs (Anandmay *et al.,* 2016)

These observations recorded in the study are in accordance with Khameneh *et al.* (2012), Anandmay *et al.* (2016), Chandrakala *et al.* (2017a) and Chandrakala et al. (2017b).

4.3.2 <u>Packed Cell Volume (%)</u>

The mean values of packed cell volume for both the groups are expressed in Table 4.11 and depicted in Fig. 4.6. ANOVA of the same has been tabulated in Table 4.12.

Table 4.11 Mean ± SE values for packed cell volume of both groups expressed in percentage

Interval / Group	Before induction	During surgery	After recovery	Pooled mean
Group A	43.25 ±2.27	43.46 ±2.04	41.96 ±2.20	42.89±0.47 ^{A}
Group B	46.45 ±2.17	46.26 ±1.47	43.03±1.39	45.25± 1.11 ^{B}
Pooled mean	44.85 ±1.57	44.86 ± 1.27	42.49 ±1.25	

Means bearing different superscripts differ significantly

Table 4.12 ANOVA for packed cell volume

Source of variation	Degrees of freedom	Sum of squares	Mean sum of squares	F cal	P value
Replications	5	435.611	87.122	8.600	0.000
Group	1	50.056	50.056	4.941*	0.036
Interval	2	44.620	22.310	2.202^{NS}	0.132
Group x Interval	2	7.678	3.839	0.379^{NS}	0.688
Error	25	253.276	10.131	-	-

NS- Non significant, *- 5% significance level

Critical Difference Values		
-	CD 5%	CD 1%
Factor A	2.186	2.957
Factor B	2.677	3.621
Treatments/(AxB)	3.786	5.122

The normal range for Packed Cell Volume in dogs is 30 to 50% (Brar *et al.,* 2014).

In the present study, pooled mean value of packed cell volume for Group A was 42.89 ± 0.47 and for Group B it was 45.25± 1.11. The average PCV value in Group A showed a variation from 43.25 ± 2.27 before induction to 41.96 ± 2.20 after recovery. While in Group B, it ranged from 46.45 ± 2.17 to 43.03 ± 1.39 respectively. Both the groups showed decreasing trend in PCV values at the end of anaesthasia.

The pooled mean value of PCV after induction for both the groups was 44.85 ±1.57 which decreased to 42.49 ± 1.25 after recovery. This decrease in PCV value in both the groups was clinically and statistically non-significant.

The overall mean value of packed cell volume was significantly higher ($p<0.05$) in Group B than Group A which might be due to splenic sequestration or due to shifting of fluids from the extravascular compartment to the intravascular compartment to maintain the cardiac output.

Similar observations are also recorded by Schricker *et al.* (2001), Ilkiw and Pascoe (2003), Pascoe *et al.* (2006) and Anandmay *et al.* (2016) Chandrakala *et al.* (2017a) , Chandrakala et al. (2017b) and Shinde *et al*. (2018).

4.3.3 Total erythrocyte count (x 10^6 /cu.mm)

The mean values for total erythrocyte count have been tabulated in Table 4.13 and depicted in Fig.4.7. ANOVA for the same has been presented in Table 4.14.

Table 4.13 Mean ± SE values for total erythrocyte count expressed in x10^6 /cu.mm

Group \ Interval	Before induction	During surgery	After recovery	Pooled mean
Group A	6.88±0.41	6.88±0.37	6.58±0.36	6.78^A ±0.10
Group B	7.44±0.45	7.44±0.34	6.88±0.30	7.25^B ±0.19
Pooled mean	7.16±0.30	7.16±0.25	6.73±0.23	

Means bearing different superscripts differ significantly at 1% significance level.

Table 4.14 ANOVA table of Total erythrocyte count

Source of variation	Degrees of freedom	Sum of squares	Mean sum of squares	F cal	P value
Replications	5	19.259	3.852	16.464	0.000
Group	1	2.016	2.016	8.619**	0.007
Interval	2	1.468	0.734	3.137^{NS}	0.061
Group x Interval	2	0.130	0.065	0.278^{NS}	0.760
Error	25	5.849	0.234	-	-

NS- Non significant, **- 1% significance level

Critical Difference Values		
-	CD 5%	CD 1%
Factor A	0.332	0.449
Factor B	0.407	0.550
Treatments/(AxB)	0.575	0.778

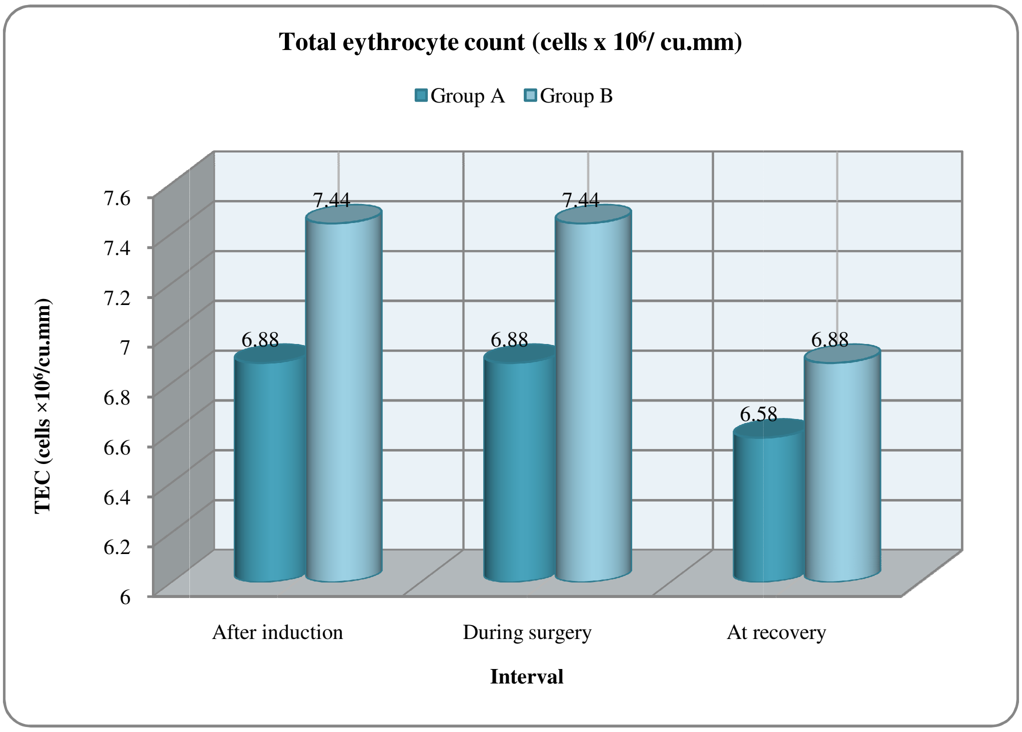


Fig. 4.7 Histogram showing the mean values of Total erythrocyte count(cells x 10^6 /cu.mm)

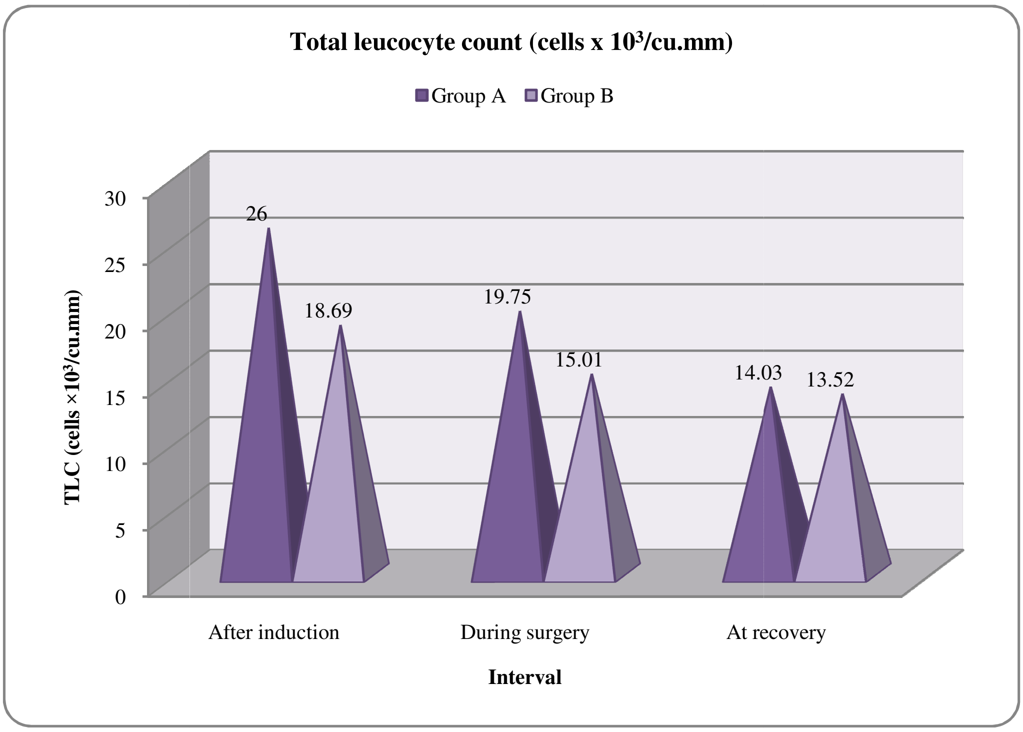


Fig. 4.8 Histogram showing the mean values of Total leucocyte count (cells × 10^3/cu.mm)

The normal range of Total Erythrocyte Count in dogs is 5 to 8 x 10^6/cu.mm (Brar *et al.,* 2014).

In Group A, the average TEC value after induction, during surgery and after recovery was 6.88 ± 0.41, 6.88 ± 0.37 and 6.58 ± 0.36 respectively with the overall mean value of 6.78 ± 0.10. The average TEC value remained unaltered during surgery and decreased thereafter recovery.

For Group B, the average values observed were 7.44 ± 0.45 after induction, 7.44 ± 0.34 during surgery and 6.88 ± 0.30 after recovery with pooled mean of 7.25 ± 0.19. Value in Group B showed similar trend observed in Group A.

The pooled mean values differed significantly ($p<0.01$) between the groups but had no clinical significance. This shows that addition of ketamine to propofol anesthesia did not affect the erythrocyte count compared to propofol infusion. Also, maintenance of anesthesia with propofol by CRI maintained in Group A did not decrease the erythrocyte count below normal limit.

The pooled mean value observed for both the groups after induction was 7.16 ± 0.3 which remained stable during surgery and then decreased after recovery to 6.73 ± 0.23. In both the groups, erythrocyte count decreased non-significantly ($p>0.05$) throughout the period of anesthesia. This decrease might be due to splenic dilation resulting in splenic sequestration of RBCs.

These observations recorded during the study corroborate with the findings of Fani *et al*. (2008), Khameneh *et al.* (2012), Anandmay *et al.* (2016) and Shinde *et al*. (2018).

4.3.4 Total Leucocyte Count (x 10^3/cu.mm)

The mean values of Total leucocyte count have been tabulated in Table 4.15 and depicted in Fig. 4.8. ANOVA for the same has been presented in Table 4.16.

Table 4.15 Mean ± SE values of total leucocyte count expressed in (x 10^3/cu.mm)

Group \ Interval	Before induction	During surgery	After recovery	Pooled mean
Group A	26.00±1.55	19.75± 1.63	14.03±2.62	19.93^{B} ±3.46
Group B	18.69±2.04	15.01±2.88	13.52±3.18	15.74^{A} ±1.54
Pooled mean	22.35^{II}±1.65	17.38^{I}±1.73	13.77^{I}±1.96	

Means bearing different superscripts differ significantly at 1% and 5% significance level.

Table 4.16. ANOVA for Total Leucocyte Count

Source of variation	Degrees of freedom	Sum of squares	Mean sum of squares	F cal	P value
Replications	5	421.247	84.249	3.438	0.017
Group	1	158.131	158.131	6.453^{*}	0.018
Interval	2	444.702	222.351	9.074^{**}	0.001
Group x Interval	2	70.806	35.403	1.445^{NS}	0.255
Error	25	612.633	24.505	-	-

*- 5% significance, ** - 1% significance, NS- Non-significant

Critical Difference Values		
-	CD 5%	CD 1%
Factor A	3.399	4.599
Factor B	4.163	5.632
Treatments/(AxB)	5.888	7.965

The normal range for Total Leucocyte Count in dogs is 6 to 16 x 10^3/cu.mm (Brar *et al.,* 2014).

In Group A, the average TLC values observed after induction 26.00 ± 1.55, during surgery 19.75 ± 1.63 and after recovery 14.03 ± 2.62 with the pooled mean of 19.93 ± 3.46. Leucocytosis was observed after induction values which might be due to pre-existing infectious causes. However, the values showed decreasing trend at the end of anaesthasia which might be due to effect of premedication with sedatives i.e. xylazine (Fani *et al*., 2008). Value at recovery was found to be returned to normal range.

In Group B, the average TLC values observed after induction, during surgery and after recovery was 18.69 ± 2.04, 15.01 ± 2.88 and 13.52 ± 3.18 with the pooled mean of 15.74 ± 1.54. The average value after induction showed marginal increase which decreased thereafter recovery to the normal range. Similarly like in Group A, this decrease in value might be due to premedication with xylazine.

The pooled mean values of both the groups differed significantly ($p<0.05$). The overall mean value for Group A 19.93 ± 3.46 was higher than that of Group B 15.74 ± 1.54. Lower value in Group B might be due to the fact that dissociating agents also reduce leukocyte counts. Ketamine and butorphanol produce analgesic effects which reduce the stress response by decrease in the plasma cortisol and adrenaline and hence was responsible for transient fall in TLC (Chandrakala *et al.,* 2017b).

These observations recorded during the study are in agreement with Fani *et al.* (2008) Anandmay *et al.* (2016) and Chandrakala *et al.* (2017b)

4.3.5 Differential Leucocyte Count

a) Neutrophils (%)

The average neutrophil values are tabulated in Table 4.17 and depicted in Fig.4.9. ANOVA for the same has been presented in Table 4.18.

Table 4.17 Mean ± SE values of Neutrophils (%) for both the groups expressed in percentage

Interval / Group	Before induction	During surgery	After recovery	Pooled mean
Group A	74.17 ± 2.79	73.27 ± 3.35	68.60 ± 3.43	72.01 ± 1.73
Group B	75.68 ± 2.71	69.72 ± 6.53	75.22 ± 3.24	73.54 ± 1.92
Pooled mean	74.93 ±1.87	71.49 ±3.54	71.91 ± 2.46	

Table 4.18 ANOVA table for Neutrophils

Source of variation	Degrees of freedom	Sum of squares	Mean sum of squares	F cal	P value
Replications	5	920.516	184.103	2.532	0.055
Group	1	21.007	21.007	0.289^{NS}	0.596
Interval	2	84.247	42.123	0.579^{NS}	0.568
Group x Interval	2	155.042	77.521	1.066^{NS}	0.360
Error	25	1818.076	72.723	-	-

NS- Non significant

Critical Difference Values		
-	CD 5%	CD 1%
Factor A	5.856	7.922
Factor B	7.172	9.703
Treatments/(AxB)	10.142	13.722

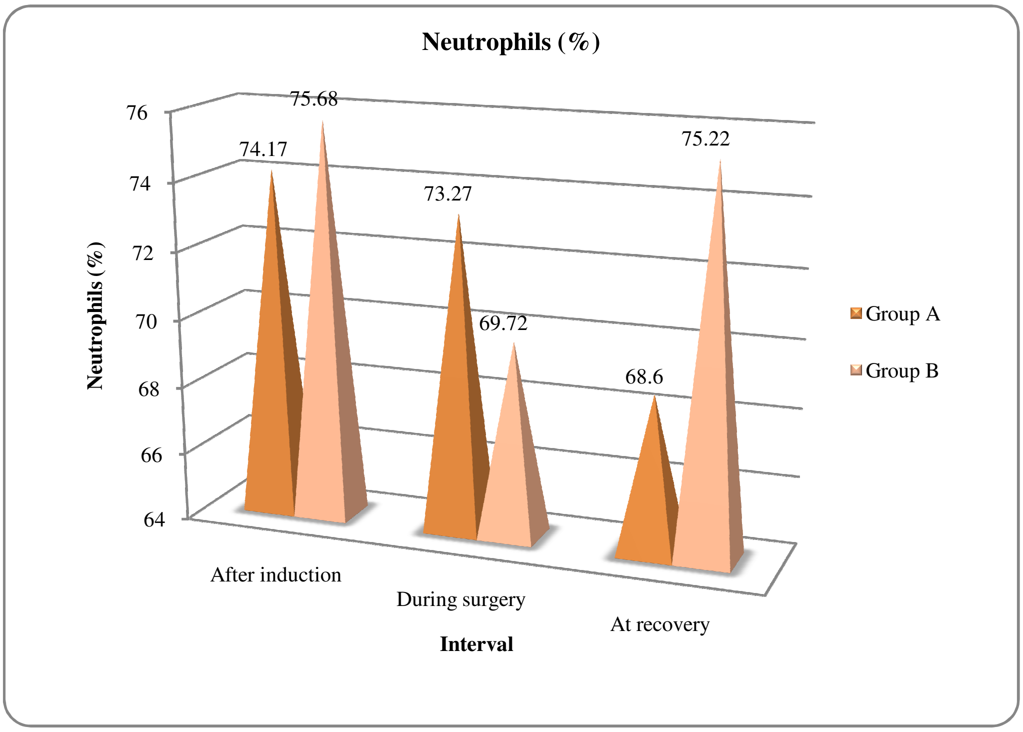


Fig. 4.9 Histogram showing the mean values of Neutrophils (%) in both the groups

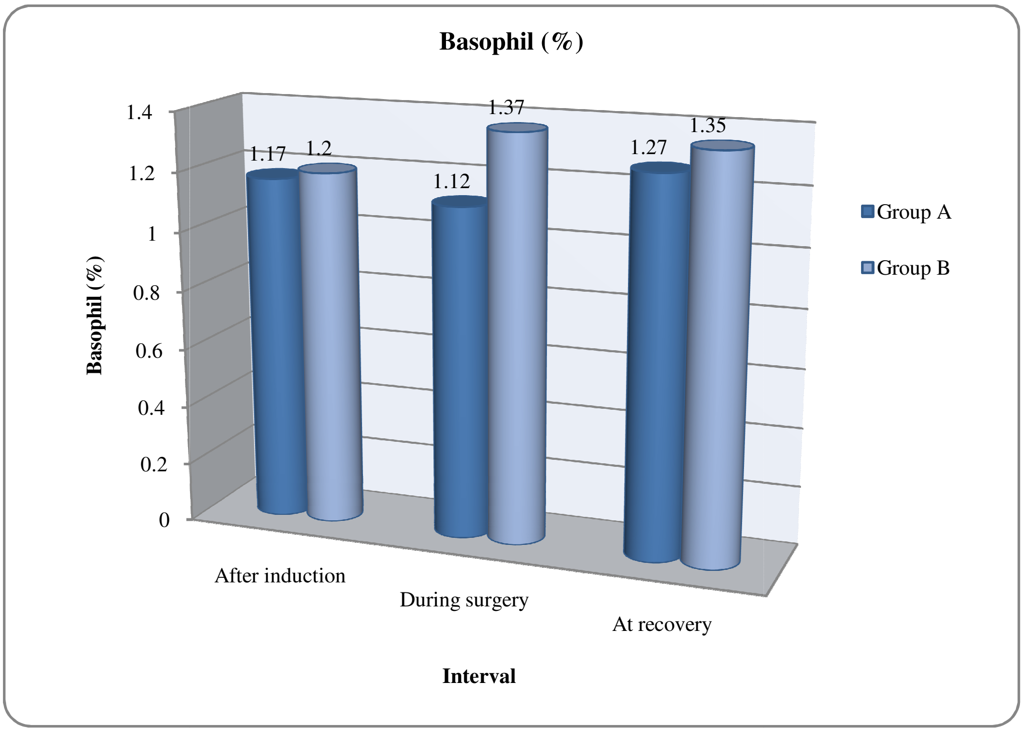


Fig. 4.10 Histogram showing mean values of Basophil (%) in both the groups

The normal range for neutrophils in dogs is 60 to 70% (Brar *et al.,* 2014).

In Group A, the average value of neutrophils observed before induction, during surgery and after recovery was 74.17 ± 2.79, 73.27 ± 3.35 and 68.60 ± 3.43 respectively with the pooled mean of 72.01 ± 1.73. A marginal neutrophilia was observed before induction values and then it decreased non-significantly over the period of anaesthasia.

In Group B, the average mean value before induction was 75.68 ± 2.71 which decreased to 69.72 ± 6.53 during surgery and again showed increase to 75.22 ± 3.24 at recovery with the pooled mean of (73.54 ± 1.92). In Group B also, patients showed mild neutrophilia before induction and at recovery. This might be due to pre-existing bacterial infection or injury.

It was observed that, the pooled mean value of Group B was numerically higher than that of Group A but there was no statistical significance between both the groups.

In group A, decreasing trend was observed from baseline value throughout the period of anaesthasia whereas in group B non-significant increase was recorded after recovery. This might be due to physiological events like increased production of epinephrine (due to fear or pain), increased heart rate and blood pressure mobilizing the neutrophils located in the margins of small vessels to enter the circulating pool.

The observations recorded during the study are in accordance with Ilkiw and Pascoe (2003), Anandmay *et al.* (2016), Chandrakala *et al.* (2017a) and Chandrakala *et al.* (2017b)

b) Basophils (%)

The average basophil values for both the groups have been tabulated below in Table 4.19 and illustrated in Fig. 4.10. ANOVA for the same has been presented in Table 4.20.

Table 4.19 Mean ± SE values of Basophils (%) for both groups expressed in percentage

Interval / Group	Before induction	During surgery	After recovery	Pooled mean
Group A	1.17 ±0.22	1.12 ±0.21	1.27 ±0.11	1.18 ± 0.04
Group B	1.20 ± 0.20	1.37 ± 0.13	1.35 ± 0.15	1.31 ± 0.05
Pooled mean	1.18 ± 0.14	1.24 ± 0.13	1.31 ± 0.09	

Table 4.20 ANOVA for Basophils

Source of variation	Degrees of freedom	Sum of squares	Mean sum of squares	F cal	P value
Replications	5	920.516	184.103	2.532	0.055
Group	1	21.007	21.007	0.289^{NS}	0.596
Interval	2	84.247	42.123	0.579^{NS}	0.568
Group x Interval	2	155.042	77.521	1.066^{NS}	0.360
Error	25	1818.076	72.723	-	-

NS- non-significant

Critical Difference Values		
-	CD 5%	CD 1%
Factor A	5.856	7.922
Factor B	7.172	9.703
Treatments/(AxB)	10.142	13.722

Basophils are rarely encountered in dogs (Brar *et al.,* 2014).

In the present study average percentage of basophils observed in Group A before induction, during surgery and after recovery was 1.17 ±0.22, 1.12 ± 0.21 and 1.27 ±0.11 respectively with pooled mean of 1.18 ± 0.04. There was an increase observed in the average basophil percentage after recovery which was both clinically and statistically non-significant.

In Group B, the average basophils percentage was 1.20 ± 0.20 before induction, 1.37 ± 0.13 during surgery and 1.35 ±0.15 after recovery with the overall mean as 1.31 ±0.05. The values showed non-significant alterations throughout the anaesthasia.

The overall mean percentage of basophil for both the groups before induction was 1.18 ± 0.14, during procedure was 1.24 ± 0.13 and 1.31 ±0.09 after recovery. The values showed clinically and statistically non-significant increase throughout the anaesthasia.

These observations recorded during the study regarding non-significant alterations in basophil count are similar with observations made by Khameneh *et al.* (2012), Anandmay *et al.* (2016), Chandrakala *et al*. (2017a) and Chandrakala *et al*. (2017b)

c) Eosinophils (%)

The average percentage values of eosinophils for both the groups have been tabulated below in Table 4.21 and depicted in Fig. 4.11. ANOVA for the same has been presented in Table 4.22.

Table 4.21 Mean ± SE values of Eosinophils (%) for both the groups expressed in percentage

Interval / Group	Before induction	During surgery	After recovery	Pooled mean
Group A	4.83 ± 1.92	4.58 ± 1.89	6.73 ± 2.26	5.38 ±0.68
Group B	4.97 ± 1.04	4.23 ± 0.73	4.87 ± 0.94	4.69 ± 0.23
Pooled mean	4.90 ± 1.04	4.41 ± 0.97	5.80 ± 1.20	

Table 4.22 ANOVA for eosinophils

Source of variation	Degrees of freedom	Sum of squares	Mean sum of squares	F cal	P value
Replications	5	142.005	28.401	2.334	0.072
Group	1	4.340	4.340	0.357^{NS}	0.556
Interval	2	11.954	5.977	0.491^{NS}	0.618
Group x Interval	2	6.534	3.267	0.269^{NS}	0.767
Error	25	304.170	12.167	-	-

NS- non significant

Critical Difference Values		
-	CD 5%	CD 1%
Factor A	2.395	3.240
Factor B	2.933	3.969
Treatments/(AxB)	4.149	5.613

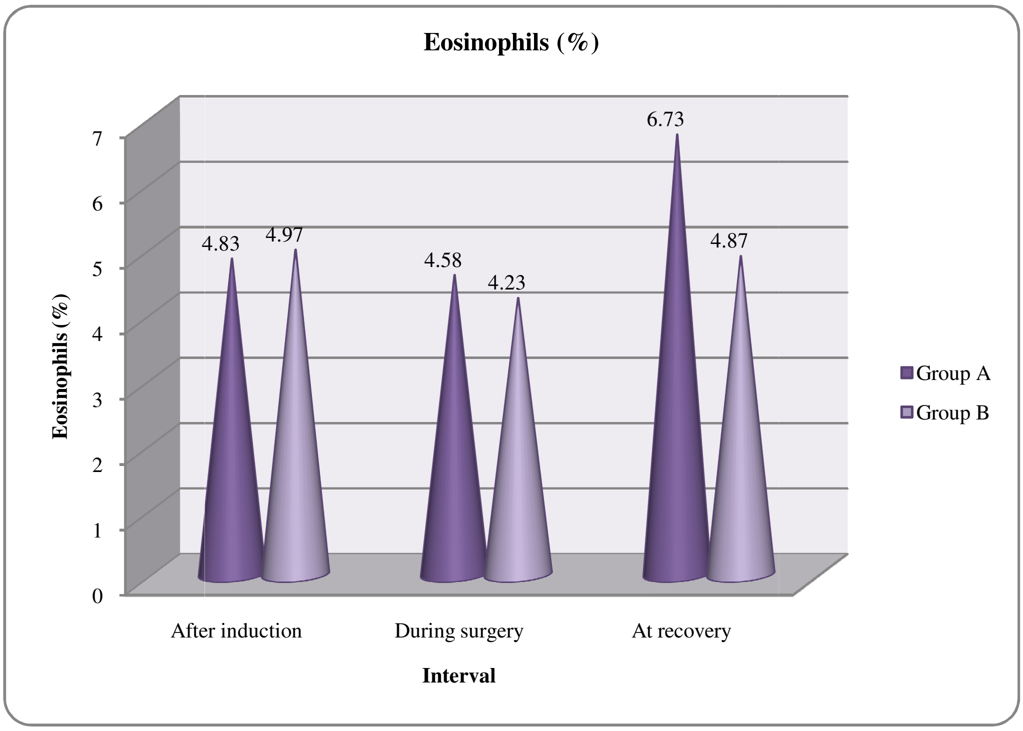


Fig. 4.11 Histogram showing the mean values of Eosinophils (%) in both the groups

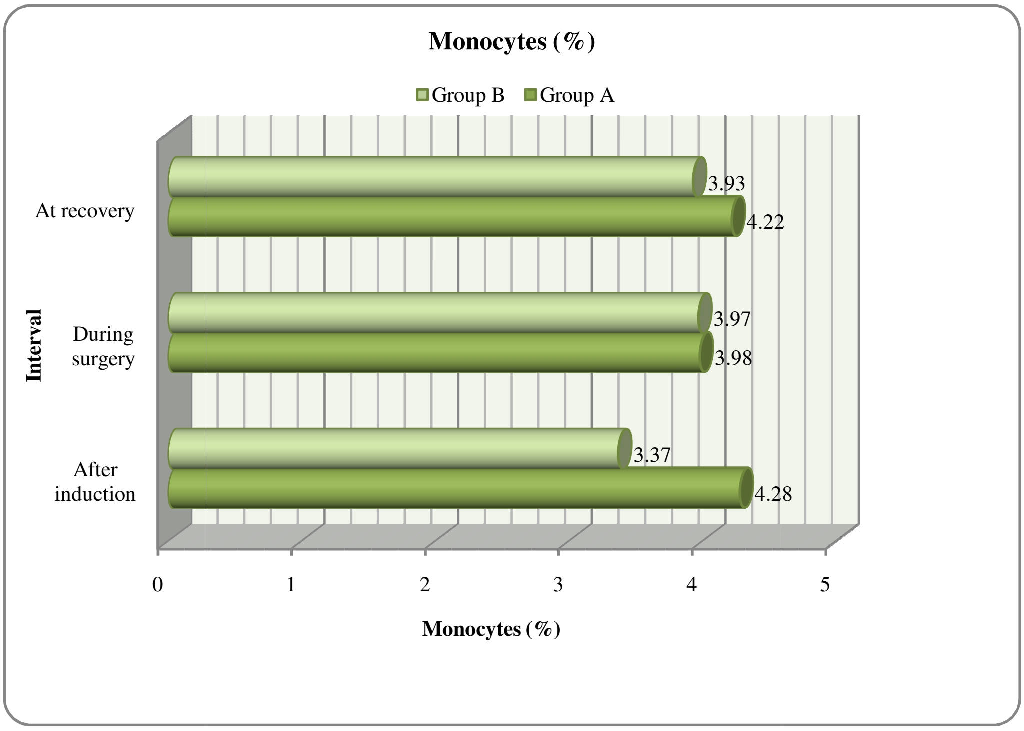


Fig. 4.12 Histogram showing the mean values of Monocytes (%) in both the groups

The normal range for eosinophils in dogs is 2 to 10% (Brar *et al.,* 2014).

It can be observed from the table that, average eosinophil percentage in Group A before induction, during surgery and after recovery was 4.83 ± 1.92, 4.58 ± 1.89 and 6.73 ± 2.26 respectively with the pooled mean of 5.38 ± 0.68. The average value increased non-significantly after recovery than pretreatment value and also it was within normal range.

In Group B, the pooled mean value was observed to be 4.69 ± 0.23 while the average values were 4.97 ± 1.04 before induction, 4.23 ± 0.73 during surgery and 4.87 ± 0.94 after recovery. All the alterations were found non-significant and within normal range.

Comparing the pooled mean values of both the groups, Group A value 5.38 ± 0.68 was observed to be higher than that of Group B 4.69 ± 0.23 which was both clinically and statistically non-significant (p>0.05).

The overall mean value observed for both the groups before induction was 4.90 ± 1.04 which decreased to 4.41 ± 0.97 during surgery and then showed increased to 5.80 ± 1.20 after recovery. Marginal decrease in value during surgery than pretreatment values might be due to acute inflammatory conditions caused due to surgical trauma

These observations recorded in the study are in accordance with Ilkiw and Pascoe (2003), Khameneh *et al.* (2012), Anandmay *et al.* (2016), Chandrakala *et al*. (2017a) and Chandrakala *et al*. (2017b).

d) Monocytes (%)

The average values of monocytes for both the groups have been tabulated below in Table 4.23 and illustrated in Fig. 4.12. ANOVA for the same has been presented in Table 4.24.

Table 4.23 Mean ± SE values of Monocytes(%) for both the groups expressed in percentage

Interval / Group	Before induction	During surgery	After recovery	Pooled mean
Group A	4.28 ± 0.96	3.98 ± 0.97	4.22 ± 1.01	4.16 ± 0.09
Group B	3.37 ± 0.82	3.97 ± 0.20	3.93 ± 0.78	3.76 ± 0.19
Pooled mean	3.83 ± 0.62	3.98 ± 0.47	4.08 ± 0.61	

Table 4.24 ANOVA table for monocytes

Source of variation	Degrees of freedom	Sum of squares	Mean sum of squares	F cal	P value
Replications	5	41.859	8.372	2.496	0.058
Group	1	1.480	1.480	0.441^{NS}	0.513
Interval	2	0.380	0.190	0.057^{NS}	0.945
Group x Interval	2	1.282	0.641	0.191^{NS}	0.827
Error	25	83.866	3.355	-	-

NS- non significant

Critical Difference Values		
-	CD 5%	CD 1%
Factor A	1.258	1.702
Factor B	1.540	2.084
Treatments/(AxB)	2.178	2.947

The normal range for monocytes in dogs is 3 to 8% (Brar *et al.,* 2014).

In Group A, the mean monocyte percentage before induction, during surgery or after recovery was observed to be 4.28 ± 0.96, 3.98 ± 0.97 and 4.22 ± 1.01 respectively with the pooled mean of 4.16 ± 0.09. Though the value decreased during surgery than pre-anesthasia value, it stabilized after recovery.

In Group B, the values observed were 3.37 ± 0.82 before induction, 3.97 ± 0.20 during surgery and 3.93 ± 0.78 after recovery with the pooled mean of 3.76 ± 0.19.

During the study, the overall mean value of monocytes observed in Group A was 4.16 ± 0.09 while in Group B it was 3.76 ± 0.19. The values showed numerical difference between the groups which was statistically non-significant.

The pooled mean value for both the groups before induction was 3.83 ± 0.62, 3.98 ± 0.47 during surgery and 4.08 ± 0.61 after recovery. An increasing trend was observed in overall mean values of both the group throughout the anaesthasia which was both clinically and statistically non-significant.

These observations recorded during the study regarding non-significant alterations in monocyte count are in accordance with Khameneh *et al.* (2012), Anandmay *et al.* (2016), Chandrakala *et al*. (2017a) and Chandrakala *et al*. (2017b)

e) Lymphocytes (%)

The mean percentage values of lymphocytes for both the groups have been tabulated below in Table 4.25 and depicted in Fig. 4.13. ANOVA for the same has been presented in Table 4.26.

Table 4.25 Mean ± SE values of Lymphocyte (%) for both the groups expressed in percentage

Interval / Group	Before induction	During surgery	After recovery	Pooled mean
Group A	14.88 ± 1.40	15.47 ± 2.00	17.80 ± 2.31	16.05 ± 0.89
Group B	14.80 ± 2.39	20.67 ± 6.38	14.70 ± 2.50	16.72 ± 1.97
Pooled mean	14.84 ± 1.32	18.07 ± 3.28	16.25 ± 1.69	

Table 4.26 ANOVA for Lymphocyte

Source of variation	Degrees of freedom	Sum of squares	Mean sum of squares	F cal	P value
Replications	5	708.455	141.691	2.927	0.033
Group	1	4.067	4.067	0.084^{NS}	0.774
Interval	2	62.737	31.369	0.648^{NS}	0.532
Group x Interval	2	105.904	52.952	1.094^{NS}	0.350
Error	25	1210.360	48.414	-	-

NS- non-significant

Critical Difference Values		
-	CD 5%	CD 1%
Factor A	4.778	6.464
Factor B	5.852	7.917
Treatments/(AxB)	8.275	11.196

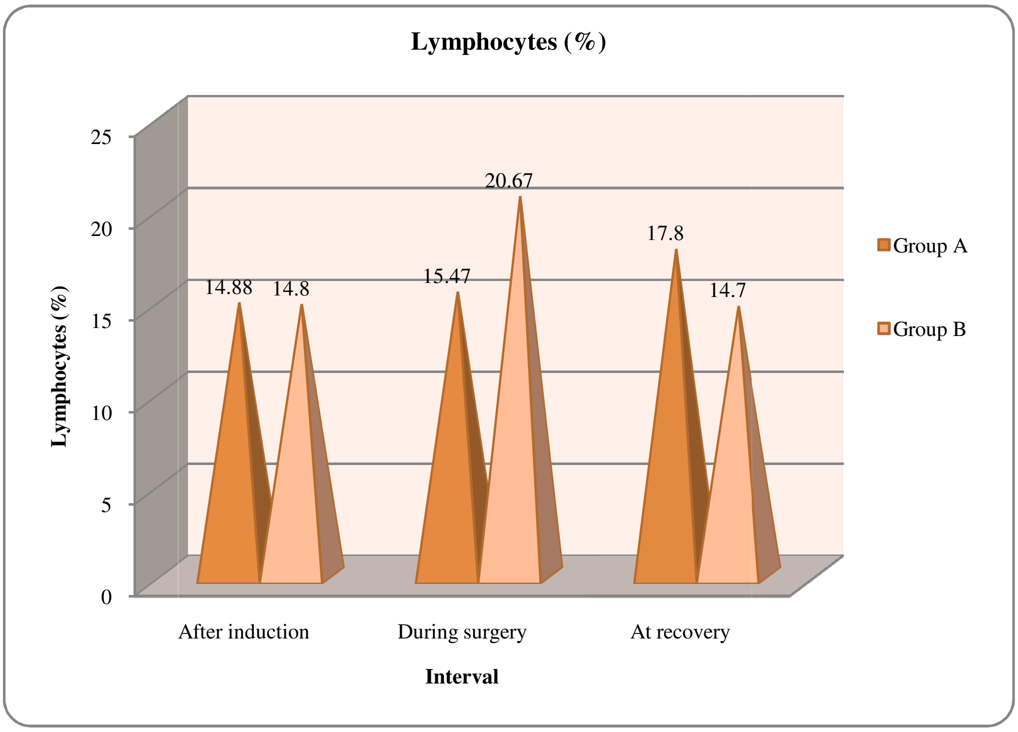


Fig. 4.13 Histogram showing the mean values of Lymphocytes (%) in both the groups

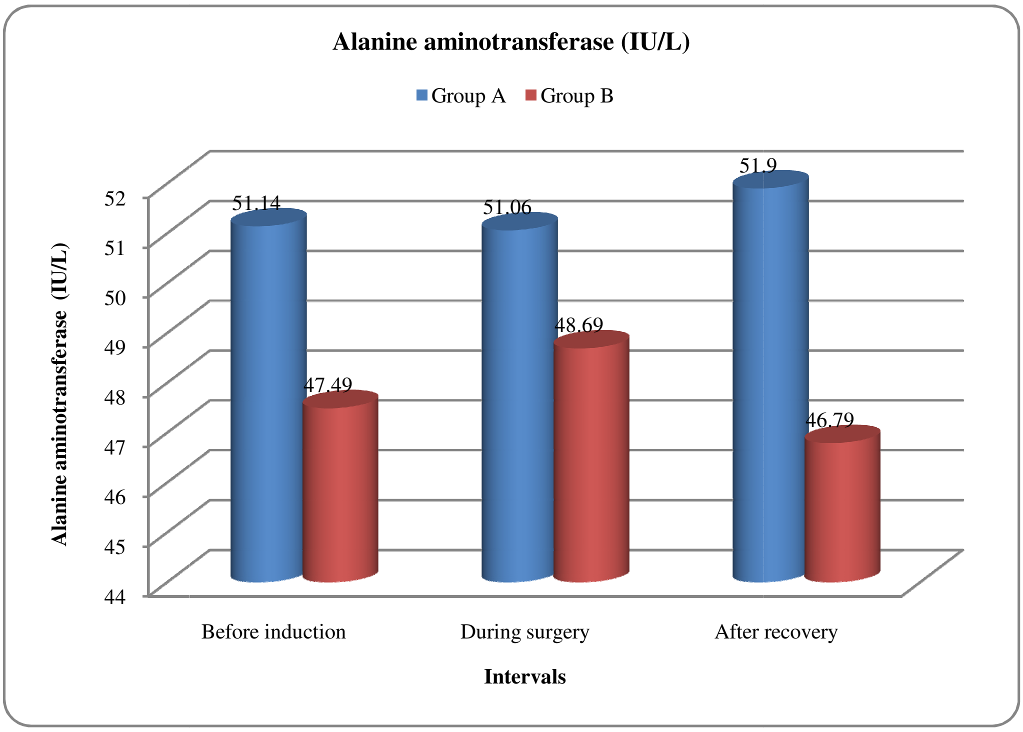


Fig. 4.14 Histogram showing the mean values of ALT (IU/L) in both the groups

The normal range for lymphocytes in dogs is 15 to 30 % (Brar *et al.,* 2014).

Group A showed an increasing trend in the average lymphocyte count before induction 14.88 ± 1.40, during surgery 15.47 ± 2.00 till recovery 17.8 ± 2.31 with the pooled mean of 16.05 ± 0.89. Pretreatment values showed mild lymphocytopenia which showed increase during surgery, however the values were within normal range and statistically significant.

In Group B, the average lymphocyte percentage observed before induction, during surgery and after recovery was 14.8 ± 2.39, 20.67 ± 6.38 and 14.7 ± 2.50 with the pooled mean of 16.72 ± 1.97. In this group, the value increased during surgery and returned to previous value after recovery. This slight increase in value during surgery in both the groups might be due to pain exhibited by the patients which subsided in Group B it continued to increase in Group A. As propofol lacks the analgesic properties, pain or excitement experienced by the patient lead to consistent increase in value which was statistically non-significant. While in Group B, addition of ketamine in small doses lead to peri-operative analgesia and hence values seemed decreasing.

The pooled mean value of lymphocyte for both the groups before induction was 14.84 ± 1.32, 18.07 ± 3.28 during surgery and 16.25 ± 1.69 after recovery. This showed that both the groups showed marginal increase in lymphocyte value during surgery which decreased thereafter recovery. All the values were both statistically and clinically non-significant.

Similar observations are also recorded by Anandmay *et al.* (2016) .

4.4 Biochemical estimation

4.4.1 Alanine amino transferase (IU/L)

The average values of ALT for both the groups at different intervals have been tabulated below in Table 4.27 and depicted in Fig. 4.14 ANOVA for the same has been presented in Table 4.28.

Table 4.27 Mean ± SE values of ALT for both the groups expressed in (IU/L)

Interval / Group	Before Induction	During surgery	After recovery	Pooled mean
Group A	51.14 ± 10.00	51.06 ± 9.77	51.90 ± 9.80	51.37 ± 0.27
Group B	47.49 ± 3.62	48.69 ± 5.25	46.79 ± 4.11	47.66 ± 0.56
Pooled mean	49.32 ± 5.10	49.87 ± 5.30	49.35 ± 5.12	

Table 4.28 ANOVA for Alanine amino transferase

Critical Difference Values		
-	CD 5%	CD 1%
Factor A	10.610	14.354
Factor B	12.994	17.580
Treatments/(AxB)	18.377	24.862

Source of variation	Degrees of freedom	Sum of squares	Mean sum of squares	F cal	P value
Replications	5	4502.448	900.490	3.772	0.011
Group	1	123.691	123.691	0.518^{NS}	0.478
Interval	2	2.352	1.176	0.005^{NS}	0.995
Group x Interval	2	11.345	5.672	0.024^{NS}	0.977
Error	25	5968.528	238.741	-	-

NS-Non-significant

The normal range for ALT in dogs is 25 to 92 IU/L. (Brar *et al.* 2014).

The average ALT value in Group A before induction, during surgery and after recovery was 51.14 ± 10.00, 51.06 ± 9.77 and 51.90 ± 9.80 respectively with the overall mean of 51.37± 0.27. The average values seemed stable throughout the anaesthasia and showed non-significant marginal alterations.

While in Group B, the values before induction, during surgery and after recovery were 47.49 ± 3.62, 48.69 ± 5.25 and 46.79 ± 4.11 with the pooled mean of 47.66 ± 0.56. The pooled mean values varied non-significantly between both the groups ($p>0.05$).

In Group A, the average values of ALT showed minimum alterations till the recovery which was clinically and statistically non-significant. It showed that constant infusion of propofol at smaller doses for longer time did not affect the liver metabolism. In Group B the value decreased non-significantly after recovery, which thought to be due to reduced cardiovascular stress by ketamine-propofol admixture as the value of ALT is mainly influenced by heart activity compared to liver.

The pooled mean value of ALT for both the groups before induction was 49.32 ± 5.10, 49.87 ± 5.30 during surgery which found to be stable at recovery 49.35± 5.32. The values explained that, ALT values remained fairly stable at all intervals in both the groups.

Similar findings are recorded by Kim and Jang (1999), Ilkiw and Pascoe (2003) and Khameneh (2012).

4.4.2 <u>Aspartate amino transferase (IU/L)</u>

The average mean values for AST have been tabulated in Table 4.29 and depicted in Fig. 4.15. ANOVA for the same has been presented in Table 4.30.

Table 4.29 Mean ± SE values of AST for both the groups expressed in IU/L

Interval / Group	Before induction	During surgery	After recovery	Pooled mean
Group A	18.04 ± 1.43	18.78 ± 1.36	16.04 ± 1.31	17.62 ± 0.82^{A}
Group B	22.30 ± 1.90	20.78 ± 2.01	18.31 ± 2.03	20.46 ± 1.16^{B}
Pooled mean	20.17 ± 1.30	19.78 ± 1.12	17.17 ± 1.20	

Means bearing different superscripts differ significantly

Table 4.30 ANOVA table for AST

Source of variation	Degrees of freedom	Sum of squares	Mean sum of squares	F cal	P value
Replications	5	136.981	27.396	1.777	0.154
Group	1	72.789	72.789	4.721*	0.039
Interval	2	63.678	31.839	2.065^{NS}	0.148
Group x Interval	2	9.073	4.536	0.294^{NS}	0.748
Error	25	385.482	15.419	-	-

*- Significant at 5% level, NS- non-significant

Critical Difference Values		
-	CD 5%	CD 1%
Factor A	2.696	3.648
Factor B	3.302	4.468
Treatments/(AxB)	4.670	6.318

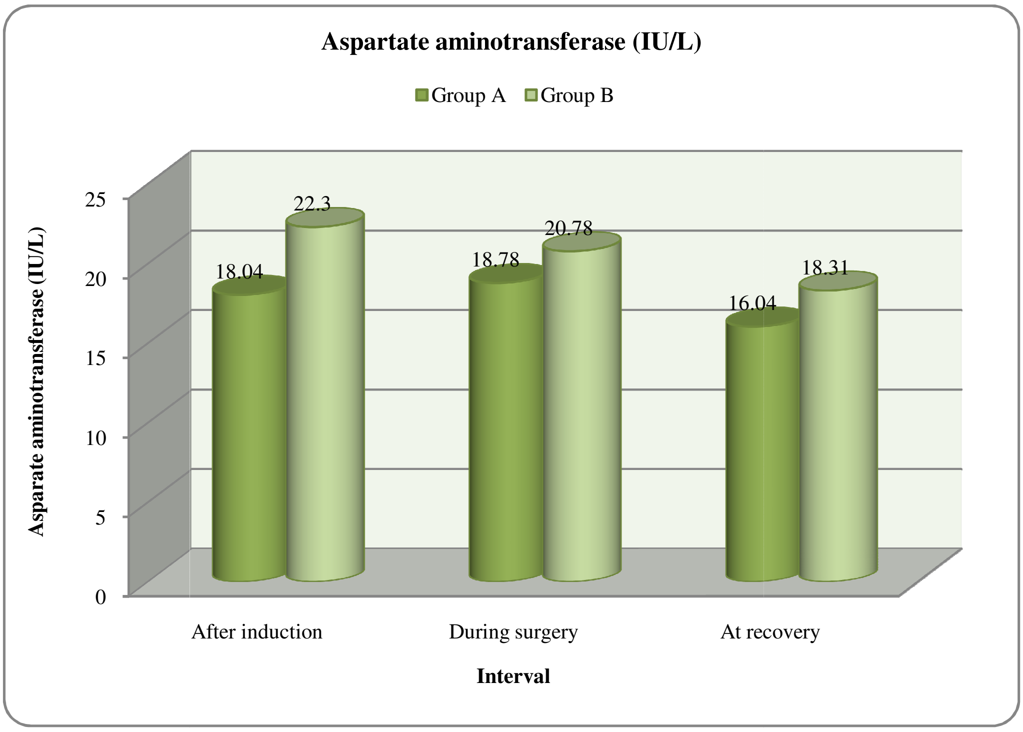


Fig. 4.15 Histogram showing the mean values of AST (IU/L) in both the groups

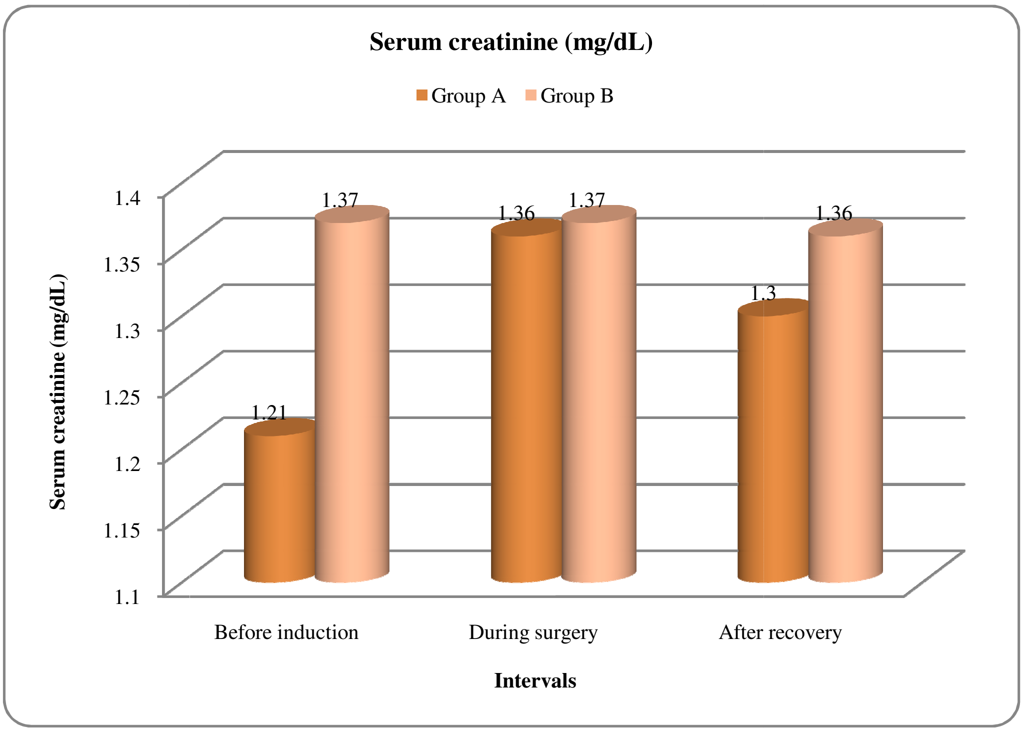


Fig. 4.16 Histogram showing the mean values of Serum creatinine (mg/dL) in both the groups

The normal range for AST in dogs is 10 to 62 IU/L (Brar *et al.,* 2014).

The average values of AST concentration in Group A varied from 18.04±1.43 before induction, 18.78 ± 1.36 during surgery and 16.04 ± 1.31 after recovery with pooled mean of 17.62 ± 0.82.

In Group B the average values before induction, during surgery and after recovery were observed to be 22.30 ± 1.90, 20.78 ± 2.01 and 18.31±2.03 with pooled mean of 20.46 ±1.16.

In both the groups, the AST concentration increased during surgery which might be due damage to muscles due to procedure or damage to liver however then decreased to normal range after recovery (Khameneh, 2012). The overall mean values differed significantly ($p<0.05$) from each other between both the groups. Comparatively higher pooled mean value was observed in Group B 20.46 ± 1.16 than Group A 17.62 ± 0.82. This may be due to addition of ketamine in propofol which might have added additional stress to liver and kidneys for elimination.

The pooled mean value of AST for both the groups before induction was observed to be 20.17 ± 1.30 which reduced to 19.78 ± 1.2 during surgery and showed further decrease after recovery to 17.17 ± 1.20. Although there was decreasing trend observed in the values, they were both clinically and statistically non-significant.

These observations recorded during the study are in accordance with Khameneh (2012), Shinde *et al.* (2018).

4.4.3 Serum creatinine – (mg/dL)

The values of serum creatinine for both the groups have been tabulated in Table 4.31 and depicted in Fig. 4.16. ANOVA for the same has been presented in Table 4.32.

Table 4.31 Mean ± SE values of Serum creatinine for both the groups expressed in mg/dL

Interval / Group	Before induction	During surgery	After recovery	Pooled mean
Group A	1.21 ± 0.10	1.36 ± 0.08	1.30 ± 0.05	1.29 ± 0.04
Group B	1.37 ± 0.09	1.37 ± 0.10	1.36 ± 0.05	1.37 ± 0.01
Pooled mean	1.29 ± 0.07	1.36 ± 0.06	1.33 ± 0.03	

Table 4.32 ANOVA of Serum creatinine

Source of variation	Degrees of freedom	Sum of squares	Mean sum of squares	F cal	P value
Replications	5	0.567	0.113	5.222	0.002
Group	1	0.054	0.054	2.462^{NS}	0.129
Interval	2	0.035	0.018	0.814^{NS}	0.455
Group x Interval	2	0.034	0.017	0.778^{NS}	0.470
Error	25	0.543	0.022	-	-

NS- non-significant

Critical Difference Values		
-	CD 5%	CD 1%
Factor A	0.101	0.137
Factor B	0.124	0.168
Treatments/(AxB)	0.175	0.237

The normal range for serum creatinine in dogs is 0.5 to 1.6mg/dL (Brar *et al.,* 2014).

The average creatinine concentration observed in Group A before induction, during surgery and after recovery was 1.21 ± 0.10, 1.36 ± 0.08 and 1.30 ± 0.05 respectively with the pooled mean of 1.29 ± 0.04. The value showed non-significant increase during surgery which might be due stress on kidneys for the elimination of propofol. However, the values were within normal range and hence there was no clinical significance.

In Group B, the value before induction was 1.37 ± 0.09, 1.37 ± 0.10 during surgery and 1.36 ± 0.05 after recovery with the pooled mean of 1.37 ± 0.01. The unaltered mean values show that addition of ketamine to propofol did not affect the kidney function.

The pooled mean value observed for both the groups before induction, during surgery and at recovery was 1.29 ± 0.07, 1.36 ± 0.06 and 1.33 ± 0.03 respectively. The values altered non-significantly within intervals in both the group with the increased value during surgery. This showed that in both the groups, there was small amount of stress for the elimination of anesthetic drugs.

Similar observations are also recorded by Okwudili *et al.* (2014) and Chandrakala *et al.* (2017b)

4.4.4 Blood urea nitrogen (mg/dL)

The average values of Blood urea nitrogen for both the groups at different intervals have been presented below in Table 4.33 and depicted in Fig. 4.17. ANOVA for the same has been tabulated in Table 4.34.

Table 4.33 Mean ± SE values of BUN for both the groups expressed in mg/dL

Interval / Group	Before Induction	During surgery	After recovery	Pooled mean
Group A	13.01 ± 3.07	15.06 ± 3.46	15.48 ± 1.79	14.51 ± 0.76^{A}
Group B	12.38 ± 2.73	10.89 ± 0.98	7.64 ± 0.58	10.31 ± 1.40^{A}
Pooled mean	12.70 ± 1.961	12.97 ± 1.823	11.56 ± 1.483	

Means bearing different superscripts differ significantly

Table 4.34 ANOVA table for BUN

Source of variation	Degrees of freedom	Sum of squares	Mean sum of squares	F cal	P value
Replications	5	560.422	112.084	6.377	0.001
Group	1	159.391	159.391	9.069^{**}	0.006
Interval	2	13.453	6.726	0.383^{NS}	0.686
Group x Interval	2	77.914	38.957	2.217^{NS}	0.130
Error	25	439.391	17.576	-	-

**- Significant at 1% level, NS-non-significant

Critical Difference Values		
-	CD 5%	CD 1%
Factor A	2.879	3.895
Factor B	3.526	4.770
Treatments/(AxB)	4.986	6.746

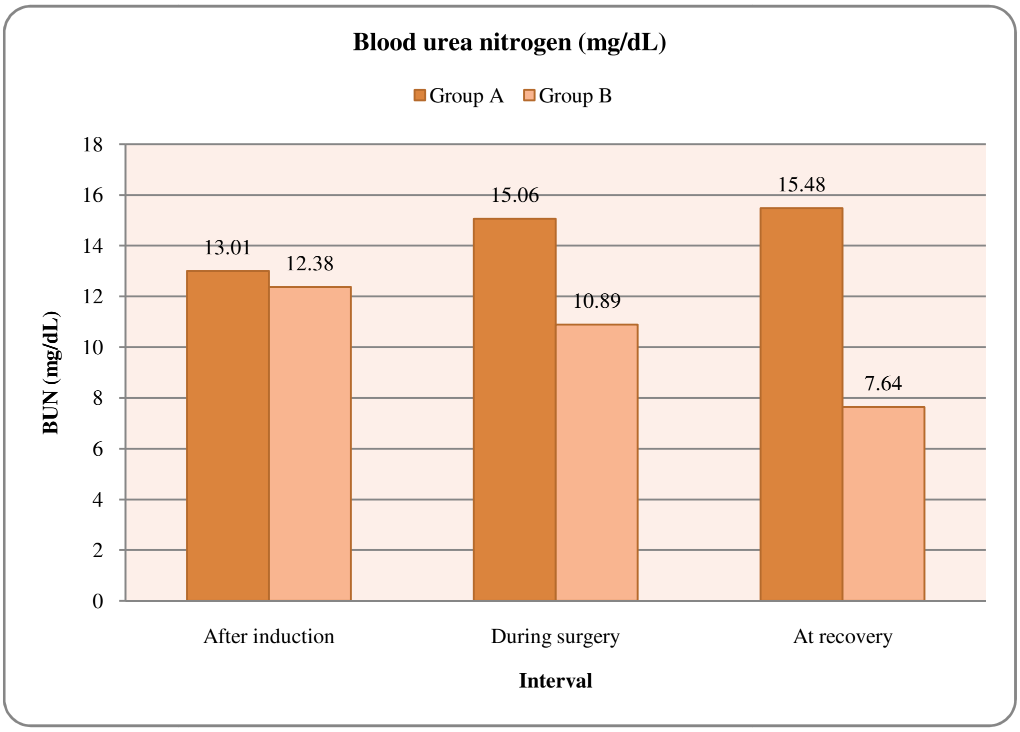


Fig. 4.17 Histogram showing the values of mean of Blood Urea Nitrogen (mg/dL) in both the groups

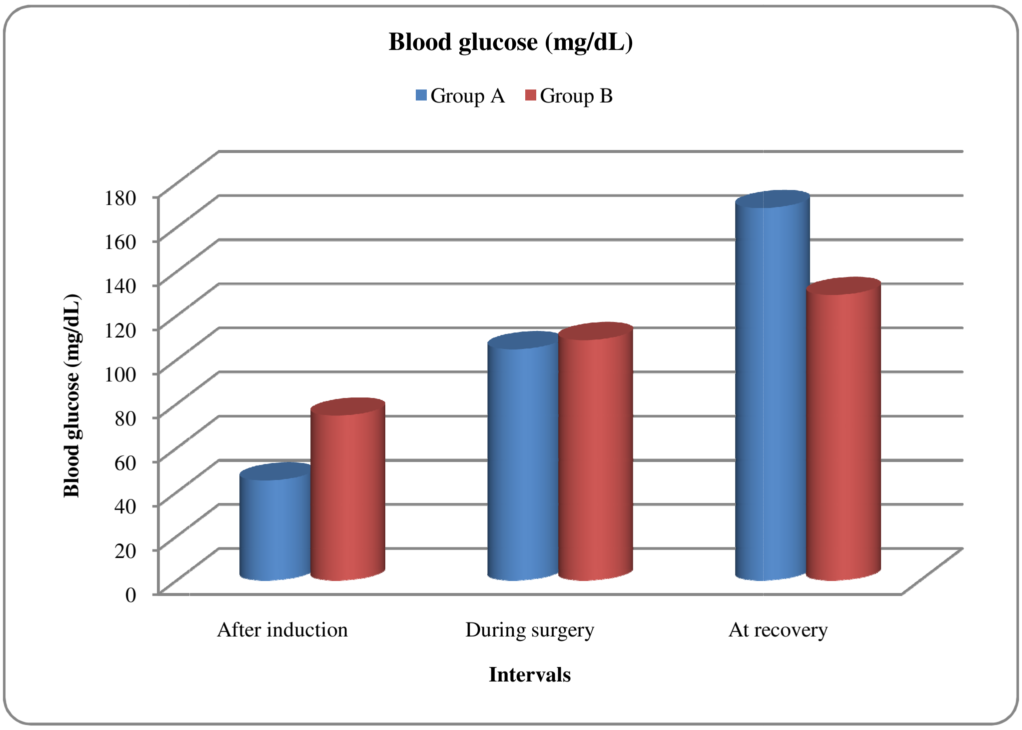


Fig. 4.18 Histogram showing the mean values of Blood glucose (mg/dL) in both the groups

The normal range for Blood Urea Nitrogen in dogs is 8 to 25 mg/dL (Brar *et al.,* 2014).

It was observed that the average BUN concentration in Group A altered from 13.01±3.07 before induction, 15.06 ± 3.46 during surgery and 15.48±1.79 after recovery with the pooled mean of 14.51 ± 0.76. These values showed non-significant increase within the intervals which might be due to hypotension and reduced renal blood flow but the values were within normal range (Singh *et al*., 2014).

In Group B, the values before induction, during surgery and after recovery were observed to be 12.38± 2.73, 10.89 ± 0.89 and 7.64± 0.58 respectively with pooled mean of 10.31 ± 1.40. Decreasing trend in the values showed stress on kidneys to eliminate ketamine from body. These alterations were within normal range except after recovery, which was non-significant.

The overall mean values of both the groups differed significantly ($p<0.01$) from each other. Higher value was found in Group A 14.51 ± 0.76 compared to Group B 10.31 ± 1.40 which might be due to propofol added stress on kidney. However, all the values were within normal range and had no clinical significance.

Blood urea nitrogen values were non-significantly elevated at the time of recovery in Group A due to faster elimination of propofol through kidneys whereas, values in Group B decreased non-significantly due to slow elimination of ketofol compared to propofol.

Similar findings are recorded by Okwudili *et al.* (2014), Singh *et al*. (2014) and Shinde *et al.* (2018)

4.4.5 <u>Blood glucose (mg/dL)</u>

The average blood glucose values at different intervals in both the groups have been tabulated in Table 4.35 and depicted in Fig. 4.18. ANOVA for the same has been presented in Table 4.36.

Table 4.35 Mean ± SE values of blood glucose for both the groups expressed in mg/dL

	After induction	During surgery	At recovery	Pooled mean
Group A	45.26 ± 5.81^{a}	104.77 ± 14.49^{b}	168.77 ± 13.54^{c}	106.26 ± 35.66
Group B	74.69 ± 16.70^{a}	108.89 ± 11.69^{b}	129.38 ± 9.46^{c}	104.32 ± 15.95
Pooled mean	59.97 ± 9.52^{I}	106.83 ± 8.90^{II}	149.07 ± 9.86^{III}	

Means bearing different superscripts differ significantly

Table 4.36 ANOVA table for Blood glucose

Source of variation	Degrees of freedom	Sum of squares	Mean sum of squares	F cal	P value
Replications	5	8029.186	1605.837	2.014	0.111
Group	1	33.989	33.989	0.043^{ns}	0.838
Interval	2	47675.333	23837.667	29.891^{*}	0.000
Group x Interval	2	7269.727	3634.863	4.558^{**}	0.021
Error	25	19937.284	797.491	-	-

*-5% significance, **- 1% significance, NS-non significant

Critical Difference Values		
-	CD 5%	CD 1%
Factor A	19.391	26.235
Factor B	23.750	32.131
Treatments/(AxB)	33.587	45.440

The normal range of blood glucose in dogs is 60-160 mg/dL (Brar *et al*., 2014)

In the present study, the average value of blood glucose in Group A was observed to be 45.26±5.81 before induction, 104.77 ± 14.49 during surgery and 168.77±13.54 after recovery with the pooled mean of 106.26 ± 35.66. The values increased significantly ($p<0.05$) towards the recovery.

In Group B, the values were 74.69 ± 16.70 before induction, 108.89 ± 11.69 during surgery and 129.38 ± 9.46 after recovery with the pooled mean value of 104.32 ± 15.95. In Group B also, the mean glucose concentration increased significantly ($p<0.05$) throughout the anaesthasia.

The pooled mean values of both the groups differed non-significantly ($p>0.05$) from each other. The pooled mean value of Group A (106.26 ± 35.66) was observed to be slightly higher than that of Group B (104.32 ± 15.95) which might be due the fact that propofol lacks analgesic properties at anesthetic doses. However, the little difference in the values of both the groups suggests that combination of propofol with an opioid analgesic i.e. butorphanol served the purpose of peri-operative analgesia.

It was observed that, pooled mean value of blood glucose was significantly increased in both the groups during the surgery to 106.83 ± 8.90 and after recovery 149.07 ± 9.86 than baseline value 59.97 ± 9.52 before induction. This increasing trend in values during surgical procedure and after recovery might be due to hyperglycemia induced by propofol infusion due to affected glucose metabolism or patients with pre-existing diabetes or propofol induced insulin resistance and also premedication with alpha-2 agonist leading to suppression of insulin release and stimulating glucagon release (Chandrakala *et al.,* 2017a and Singh *et al*., 2014)

These observations recorded during the study regarding increased blood glucose levels during surgery are in accordance with Desborough (2000), Schricker *et al.* (2001), Yasuda *et al.* (2013), Njoku (2015), Chandrakala *et al.* (2017a) and Maeda *et al*. (2018).

CHAPTER V

SUMMARY AND CONCLUSION

The present study entitled "Anesthetic Efficacy of Propofol and Ketamine-Propofol Admixture with Butorphanol as Constant Rate Infusion using Fluid Bag Technique in Dog" was undertaken on 12 clinical cases of dogs presented for elective ovariohysterectomy at Teaching Veterinary Clinical Complex, Post Graduate Institute of Veterinary and Animal Sciences, Akola to evaluate the anesthetic efficacy of ketamine-propofol combination in 1:1 ratio and propofol with butorphanol as constant rate infusion for maintenance of anaesthasia.

All clinical cases were fasted for 8-10 hours and water was withheld for 6 hours prior to the induction of anesthesia to avoid vomiting and aspiration due to side effects sedatives and anesthetics in all the dogs.

These cases were randomly divided into two equal groups irrespective of age, breed and weight. All dogs were pre-medicated with Inj. xylazine @ 2 mg/kg I/M, Inj. meloxicam @ 0.3 mg/kg, and Inj. amoxicilin+cloxacilin @10 mg/kg, Inj. chlorpheniramine maleate @ 0.4 mg/kg all intramuscularly.

Dogs in Group A were induced with Inj. propofol @4 mg/kg b.wt and Inj. diazepam @0.25 mg/kg intravenously. Maintenance of anaesthasia was done by constant infusion of propofol @6 mg/kg/hr and Inj. butorphanol @0.3 mg/kg/hr. Dogs in Group B were induced with ketamine-propofol admixture (1:1) @4 mg/kg b.wt. and Inj. diazepam @0.25 mg/kg intravenously. They were maintained with same admixture at 6 mg/kg/hr and Inj. butorphanol @0.3 mg/kg/hr.

In the present study, for the maintenance of anesthesia in both the groups the calculated amount of anesthetic drug was added to a normal saline bag of 250 ml capacity after withdrawing the same quantity. The constant infusion was maintained at the flow rate of 5 ml/kg/hr.

Anesthetic efficacy of both the treatment protocols was judged based upon the quality of anesthesia, clinico-physiological parameters and hemato-biochemical parameters estimations at different intervals. To evaluate the quality of anesthesia, various reflexes *viz*., jaw-tone, pedal reflex, position of eye balls, palpebral reflexes were checked during the period of anaesthasia. All the dogs from both the groups were in a surgical plane of anaesthasia and did not show pain response on painful surgical stimuli. The above mentioned reflexes were absent till the end of infusion. Recovery time was determined as the time required from the end of infusion till the head lifting of patient. There was a significant difference between the recovery times observed in both the groups. The patients from Group B showed faster recovery than that of Group A.

Clinico-physiological parameters were recorded before induction, after induction, during surgery (at 30 min) and after recovery. Rectal temperature of dogs from Group A (101.10 ± 0.17) was higher than that of Group B (100.7 ±0.40) and showed statistical significance ($p<0.05$) but had no clinical relevance. Respiratory rate of dogs undergoing propofol infusion was (19.04 ± 2.22) and (16.63 ± 1.94) in dogs undergoing ketamine and propofol admixture infusion. Though the respiration rate was statistically significant ($p<0.05$) between the intervals in both the groups, it was well maintained within the normal physiological limit throughout the period of anaeshasia. Heart rate was higher in Group B (70.00 ±10.04) than Group A (54.38 ±2.97). The overall pooled mean values of heart rate between the groups differed significantly at 5% level of significance.

For the hematological estimations, blood samples were collected before induction, during surgical procedure (at 30 min) and at recovery. A non-significant ($p>0.05$) decrease in haemoglobin was observed in both the groups which was within normal range. PCV value differed significantly between both the groups which thought to be of pre-operative withholding of water intake or shifting of fluid from extravascular compartment to intravascular compartment. The mean values for TEC differed significantly ($p<0.01$) between the groups but had no clinical relevance. The pooled mean value of TLC observed in Group A (19.93 ± 3.46) was significantly higher ($p<0.05$) than that of Group B (15.74 ±1.54). This higher value might be due pain experienced during the surgical procedure. In differential leucocyte count, the overall neutrophil, basophil, eosinophil, monocytes and lymphocytes values showed non-significant changes ($p>0.05$) in both the groups.

Biochemical estimation was carried out before induction, during surgical procedure (at 30min) and at recovery. The overall ALT values in all the dogs from both the groups did not show any significant variation in between. The average values of AST concentration in Group A was (14.51± 0.76) which differed significantly ($p<0.05$) from Group B (10.31±1.40). This might be due to addition of ketamine in propofol in Group B which might have added additional stress to liver and kidneys for elimination and thus decreasing the value. Although, both the pooled mean values were within normal physiological range. Serum creatinine values were higher in Group B (1.37±0.01) than Group A (1.29±0.04) but they differed non-significantly ($p>0.05$) from each other. Similarly, overall BUN values were observed to be higher in Group A (14.51± 0.76) than Group B (10.31± 1.40) which differed significantly from each other at 1% significance level. Blood glucose values differed non- significantly between the groups but significantly within intervals at 1% significance level with observed pooled mean value in Group A (106.26 ± 35.66) and Group B (104.32 ± 15.95).

In the present study, in Group A total anaesthasia used for maintenance was 30 ml of Propofol and 7.5 ml of Butorphanol which was sufficient for four female dogs in a day while in Group B, 15 ml Propofol, 7.5 ml Butorphanol and 3 ml ketamine was used for four females.

Conclusion

- Considering cost-effectiveness, early and smooth recovery, ketamine-propofol admixture (1:1) at the dose rate of 6 mg/kg/hr and butorphanol at the dose rate of 0.3 mg/kg/hr by Constant Rate Infusion using Fluid Bag Technique proved to be better option for maintenance of anaesthasia.

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VITA

The author of this dissertation **Bhave Neha Prasad** was born on 9^{th} August 1994 at Ahmednagar District of Maharashtra State.

She successfully passed her Secondary School Certificate (S.S.C.) Examination in the year 2010 with distinction from N.M.V. Girls' High School, Sadashiv Peth, Pune and Higher Secondary School Certificate (H.S.S.C.) Examination in the year 2012 with First division, from S.P. College, Pune. She joined B.V.Sc & A.H. degree course in the year 2012 at Krantisinha Nana Patil College of Veterinary Sciences, Shirwal of Maharashtra Animal and Fishery Sciences University, Nagpur and successfully completed the degree course with First Division in the year 2017.

She participated actively in Inter University Sports (Ashwamedh) and National Service Scheme (N.S.S.) during her graduation. She presented a clinical case of 'Management of Paraplegia in a Kitten' in 8^{th} Clinical Case Conference on Farm and Companion Animal Practice for Veterinary Students held at Madras Veterinary College, Chennai and received First Rank in medicine section. She joined the M.V.Sc. degree programme in the discipline of Veterinary Surgery and Radiology in the year 2017 at Post Graduate Institute of Veterinary and Animal Sciences, Akola of Maharashtra Fishery and Animal Sciences University, Nagpur. She has actively participated in 41^{st} Annual Congress of Indian Society for Veterinary Surgery and National Symposium on 'New Horizons in Cancer Research pertaining to effect on Health, Production and Reproduction in Animals' held at College of Veterinary Science, Tirupati in the year of 2017.

During post graduation she has participated in 2^{nd} Clinical Case Conference in the year of 2018 organized at PGIVAS, Akola and presented a case of 'Successful Surgical Management of Contracted Tendon in a Calf' and bagged Third prize. She also attended 3^{rd} Clinical Case Conference and presented a case of 'Successful Surgical Management of Cystolith in a Pomeranian Bitch' and bagged 2^{nd} prize. She also actively participated during many cultural activities and competitions organized at her institute during her post-graduation.

THESIS ABSTRACT

a) **Title of the thesis**	:	**ANAESTHETIC EFFICACY OF PROPOFOL AND KETAMINE-PROPOFOL ADMIXTURE WITH BUTORPHANOL AS CONSTANT RATE INFUSION USING FLUID BAG TECHNIQUE IN DOG**
b) **Full name of student**	:	**Bhave Neha Prasad**
c) **Name and address of Major advisor**	:	**Dr. M. G. Thorat** Associate Professor, Department of Veterinary Surgery and Radiology, Post Graduate Institute of Veterinary and Animal Sciences, Akola
d) **Degree to be awarded**	:	M.V.Sc. (Vet. Surgery and Radiology)
e) **Year of award of degree**	:	2019
f) **Major subject**	:	Veterinary Surgery and Radiology
g) **Total number of pages in the thesis**	:	100
h) **Number of words in the abstract**	:	282
i) **Signature of Student**	:	
j) **Signature, Name and address of forwarding authority**	:	

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ABSTRACT

The present study was conducted on 12 clinical cases of female dogs that underwent elective ovariohysterectomy for the assessment of Anaesthetic Efficacy of Propofol and Ketamine-Propofol Admixture with Butorphanol as Constant Rate Infusion using Fluid Bag Technique presented to Teaching Veterinary Clinical Complex, Post Graduate Institute of

Veterinary and Animal Sciences, Akola. These clinical cases were divided into two equal groups each viz., Group A and Group B irrespective of age, breed and body weight. Quality of anaesthasia was satisfactory in both the groups and all the dogs were in surgical plane of anaesthasia. Dogs from Group A showed longer recovery time than that of Group B. A significant difference in the pooled mean values of rectal temperature, respiration rate and heart rate was observed ($p<0.05$) between the groups. In haematological parameters TEC, TLC and PCV values were statistically significant whereas rest of the parameters were non-significantly altered. There was no significant difference observed in ALT, Serum creatinine values of both the groups. AST, BUN and Blood glucose values varied significantly but were within normal limits. In Group A, total 30 ml of propofol and 7.5 ml of butorphanol was required for maintenance which was sufficient for four females i.e. approximately 7.5 ml of propofol excluding for induction dose was used for a procedure lasting for 60 minutes. Similarly in Group B, 15ml of propofol, 3ml of ketamine and 7.5 ml of butorphanol was required for four females. On the basis of observations of this study it can be concluded that, constant rate infusion using ketamine-propofol admixture with butorphanol as a part of balanced anaesthasia using fluid bag technique is better option for maintenance of anaesthasia for major or minor surgical procedures.

<u>प्रबंध सारांश</u>

१.	**प्रबंधाचे शिर्षक**	: श्वानांमध्ये ब्युटॉरफिनॉल सोबत प्रोपोफॉल व किटॅमिन-प्रोपोफॉल यांचे संयोजन करून सलाईनद्वारा स्थिर दराने संपूर्ण बधिरीकरणाच्या कार्यक्षमतेचे परीक्षण
२.	**विद्यार्थ्याचे पूर्ण नांव**	: **भावे नेहा प्रसाद**
३.	**मुख्य मार्गदर्शकाचे नांव व पत्ता**	: **डॉ. एम. जी. थोरात** सहयोगी प्राध्यापक, पशुशल्यचिकित्सा व क्ष-किरणशास्त्र विभाग, स्नातकोत्तर पशुवैद्यक व पशुविज्ञान संस्था, अकोला.
४.	**प्रदान केली जाणारी पदवी**	: एम.व्ही.एसस्सी.
५.	**पदवी प्रदान करण्याचे वर्ष**	: २०१९
६.	**मुख्य विषय**	: पशुशल्यचिकित्सा व क्ष-किरणशास्त्र
७.	**प्रबंधामधील एकुण पाने**	: १००
८.	**प्रबंध सारांशामधील एकुण शब्द**	: २५१
९.	**विद्यार्थ्याची सही**	:
१०.	**प्रबंधक कार्यवाहीस्तव पाठविणाऱ्या अधिकाऱ्याची सही, नाव व पत्ता**	:

(डॉ. एम. जी. थोरात)
प्राध्यापक तथा विभाग प्रमुख
पशुशल्यचिकित्सा व क्ष-किरणशास्त्र विभाग
स्नातकोत्तर पशुवैद्यक व पशुविज्ञान संस्था,
अकोला.

सारांश

सदर संशोधनात्मक अभ्यासक्रम हा पशुसर्वचिकित्सालयीन शैक्षणीक संकुल, अकोला येथे नसबंदी शस्त्रक्रियेसाठी, आलेल्या बारा मादी श्वानांमध्ये संपूर्ण बधिरीकरणासाठी प्रोपोफॉल आणि किटॅमिन- प्रोपोफॉल यांचे १:१ गुणोत्तरामध्ये सयोंजन करून ब्युटॉरफिनॉल सोबत बधिरीकरण करण्याच्या कार्यक्षमतेची परीक्षण करण्यासाठी हाती घेण्यात आला. ह्या सर्व श्वानरुग्णांची दोन समान गटांमध्ये विभागणी करण्यात आली. दोन्ही गटांमधील श्वानांमध्ये बधिरीकरणाची गुणवत्ता समाधानकारक आढळून आली परंतु गट 'अ' मधील श्वानांमध्ये गट 'ब' पेक्षा

बधिरीकरणातून बाहेर येण्यास वेळ जास्त लागल्याचे निदर्शनास आले. सदर अभ्यासक्रमाच्या कालावधी दरम्यान दोन्ही गटांमधल्या श्वानांचे चिकित्सालयीन निरीक्षण, रक्तनमुन्यांची चाचणी व जीवरसायनिक चाचणी वेळोवेळी करण्यात आल्या. संपूर्ण बधिरीकरणाच्या कालावधीमध्ये हृदयाचे ठोके, श्वसन दर व शरीर तापमानमध्ये दोन्ही गटामध्ये चढउतार दिसून आले. परंतू सर्व बदल मर्यादीत पातळीमध्ये असल्याचे आढळून आले. रक्तनमुन्यांच्या चाचण्यांमध्ये तांबड्या पेशी, पांढऱ्या पेशी व पीसीव्ही च्या पातळीमध्ये लाक्षणिक चढउतार आढळून आले. बाकी सर्व घटकांचे प्रमाण मर्यादीत पातळीमध्ये आढळून आले. रक्तजल तपासणीअंतर्गत दोन्ही गटांमध्ये एएलटी व क्रिॲटिनीनच्या पातळीमध्ये अलाक्षणीक बदल दिसून आले. गट 'अ' मध्ये बीयुएन व ऐएसटी च्या पातळीमध्ये तर गट 'ब' मध्ये रक्तजल ग्लुकोज च्या पातळीमध्ये तुलनेने लाक्षणिक वाढ दिसुन आली. ग्लुकोज वगळता सर्व जीवरसायनीक बदल मर्यादित पातळीमध्ये आढळून आले. परंतु संख्यात्मक द्रुष्टीने महत्त्वाचे आढळून आले नाहीत. गट 'अ' मध्ये साधारण चार मादी श्वानांसाठी ३० मि. ली. प्रोपोफॉल व ७.५ मि.ली. ब्युटॉरफिनॉल तर गट 'ब' मध्ये १५ मि.ली. प्रोपोफॉल, ३ मि.ली. किटॅमिन व ७.५ मि.ली. ब्युटॉरफिनॉल यांचा वापर ४ श्वानांसाठी साधारण ६० मिनिटांच्या शस्त्रक्रियेसाठी करण्यात आला.

सदर संशोधनातुन असा निष्कर्ष निघतो की, मादी श्वानांमध्ये नसबंदीच्या शस्त्रक्रियेसाठी किटॅमिन व प्रोपोफॉल यांचे १:१ गुणोत्तरामध्ये संयोजन करून ब्युटॉरफिनॉल सोबत द्रव पिशवीमधून स्थिर दर ठेवून लहान व मोठ्या शस्त्रक्रियेसाठी वापरल्या जाऊ शकतो.