EVALUATION OF ANAESTHETIC REGIMEN USING BUTORPHANOL AND XYLAZINE/DEXMEDETOMIDINE AS PREANAESTHETICS, PROPOFOL AS INDUCTION AGENT AND ISOFLURANE AS MAINTENANCE ANAESTHETIC IN DOGS

By

VANKAR HARDIKKUMAR VISHNUBHAI

B. V. Sc.& A. H.

Registration No: 2040419013

DEPARTMENT OF VETERINARY SURGERY AND RADIOLOGY

COLLEGE OF VETERINARY SCIENCE & ANIMAL HUSBANDRY

KAMDHENU UNIVERSITY

NAVSARI-396 450

GUJARAT STATE

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Student	**Major Guide**
Vankar Hardikkumar Vishnubhai	**Dr. S. K. Jhala**

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ABSTRACT

The present clinical study was carried out on 12 clinical cases presented for surgical intervention and were divided into two different groups of six animals each. All dogs were premedicated with butorphanol @ 0.2 mg/kg, BW intramuscularly followed by intravenous administration of dexmedetomidine @ 5 µg/kg in group I and xylazine @ 0.5 mg/kg BW in group II. Induction of anaesthesia was achieved by intravenous injection of 1% propofol till effect and maintained by isoflurane in both the groups. Anaesthetic, clinico-physiological and haemato-biochemical parameters were recorded and evaluated at different time intervals during the study period.

The mean induction dose of propofol was 0.90±0.13 and 1.29±0.26 mg/kg in group I and II, respectively. Quality of sedation was excellent with smooth induction and recovery without any complication. Both the combinations produced adequate analgesia, muscle relaxation and sufficient anaesthetic depth to perform surgery.

All clinico-physiological parameters were within normal limits and no significant difference was observed between the groups. Rectal temperature was significantly decreased after induction of anaesthesia in group I and prior to induction in group II. Respiration rate decreased gradually and significantly after premedication which remained lower than base line value up to the end of observations period in both the groups; however, SpO_2 values remained non-significant throughout the study period in both the groups. Pulse rate was reduced significantly after preanaesthetic administration which gradually and non-significantly returned to near base line value at 50 minutes in both the groups. Non-significant difference was observed in the mean values of systolic blood pressure in group I and significant decrease in group II after 40 minutes of induction. Diastolic blood pressure was significantly reduced after induction in group I and 30 minutes after induction in group II; whereas, mean arterial blood pressure showed significant decrease after 20 minutes of induction in group I and 40 minutes of induction in group II.

Haematological study revealed significant decrease in mean values of haemoglobin and PCV in group I; while, non-significant decrease was observed in group II after induction of anaesthesia. Non-significant differences were observed in mean values of total erythrocyte count, total leukocyte count, neutrophils,

lymphocytes, monocytes and eosinophils at differential intervals after administration of anaesthesia in the both groups.

Blood glucose level increased significantly at 15, 30 and 45 minutes after induction of anaesthesia in both the group. Plasma biochemical parameters revealed no significant difference between the groups. Gradual and significant decrease in mean values of total protein was observed in both the groups however; ALT values differed non-significantly. Blood urea nitrogen showed non-significant increase whereas, creatinine showed significant increase up to end of observation when compared to base values in both the groups.

KAMDHENU UNIVERSITY, GANDHINAGAR
College of Veterinary Science & A. H., Navsari

CERTIFICATE-I

Date:

This is to certify that the thesis entitled " **EVALUATION OF ANAESTHETIC REGIMEN USING BUTORPHANOL AND XYLAZINE/DEXMEDETOMIDINE AS PREANAESTHETICS, PROPOFOL AS INDUCTION AGENT AND ISOFLURANE AS MAINTENANCE ANAESTHETIC IN DOGS**" submitted for the degree of M.V.Sc. in the subject of **VETERINARY SURGERY AND RADIOLOGY** embodies bonafide research work carried out by **VANKAR HARDIKKUMAR VISHNUBHAI** under my guidance and supervision and that no part of this thesis or research work has been submitted for any other degree. The assistance, guidance and help received during the course of investigation have been fully acknowledged.

Head of the Department **Major Advisor**

Principal / Dean

Principal
College of Veterinary Science & A.H.
Kamdhenu University
Navsari - 396 450

KAMDHENU UNIVERSITY, GANDHINAGAR

College of Veterinary Science & A. H., Navsari

CERTIFICATE-II

Date:

This is to certify that the thesis entitled **EVALUATION OF ANAESTHETIC REGIMEN USING BUTORPHANOL AND XYLAZINE/DEXMEDETOMIDINE AS PREANAESTHETICS, PROPOFOL AS INDUCTION AGENT AND ISOFLURANE AS MAINTENANCE ANAESTHETIC IN DOGS** submitted by **VANKAR HARDIKKUMAR VISHNUBHAI** to the Kamdhenu University, Gandhinagar, in partial fulfilment of the requirements for the degree of M. V. Sc. in the subject of **VETERINARY SURGERY AND RADIOLOGY**, after incorporating the suggestions and recommendations made by external examiner as discussed and defended by the candidate before the thesis Examination Committee. The performance of the candidate in the oral examination has been found satisfactory; we therefore, recommend that the thesis be approved. All the corrections / modifications were made in the thesis as suggested during in the oral examination held on 01/10/2021. The corrected final copies of the thesis were submitted on _____.

Major Guide

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Place : Navsari
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(H. V. Vankar)

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LIST OF SYMBOLS AND ABBREVIATIONS

SYMBOLS		
α	:	Alpha
%	:	Per cent
@	:	at the dose rate of
β	:	Beta
ºF	:	Degree Fahrenheit
ºC	:	Degree Celsius

ABBREVIATIONS		
µg/kg	:	microgram per kilogram
ALT	:	Alanine Amino Transferase
ANOVA	:	Analysis of variance
ASA	:	American Society of Anesthesiologist
BUN	:	Blood Urea Nitrogen
BW	:	Body weight
cu.mm	:	Cubic millimeters
CRI	:	Continuous Rate Infusion
DBP	:	Diastolic Blood Pressure
DNMRT	:	Duncan Multiple New Range Test
dl	:	Deciliter
DLC	:	Differential Leukocyte Count
EDTA	:	Ethylene Diamine Tetra Acetic Acid
et al.	:	And associates
g	:	Gram
GABA	:	Gama Amino Butyric Acid
Hb	:	Haemoglobin
IM	:	Intramuscular
IV	:	Intravenous
Inj.	:	Injection
IU	:	International Unit

MAC	:	Mean Alveolar Concentration
MAP	:	Mean Arterial Pressure
mg/kg	:	milligram per kilogram
ml	:	Milliliter
mm Hg	:	Millimeter of mercury
No.	:	Number
PCV	:	Packed Cell Volume
RBC	:	Red Blood Cells
SPSS	:	Statistical Package for Social Sciences
WBC	:	White Blood Cells
SBP	:	Systolic Blood Pressure
SE	:	Standard Error
SpO_2	:	Saturation of peripheral oxygen
TEC	:	Total Erythrocytes Count
TLC	:	Total Leukocytes Count
TIVA	:	Total Intra Venous Anaesthesia
Viz.;	:	Namely

CHAPTER 1

INTRODUCTION

Anesthesia is defined as a state of unconsciousness produced by a process of controlled reversible drug-induced intoxication of the central nervous system (Muir *et al.*, 2000). Anaesthesia is induced by drugs that depress the activity of nervous tissue locally, regionally or within CNS. The term anaesthesia, derived from Greek word "anaisthaesia" meaning insensibility, is used to describe the loss of sensation to the entire or any part of the body (Thurmon and Short, 2007). Animals under general anaesthesia have reduced sensitivity and motor responses to external noxious stimuli (Welsh, 2009). Minor surgical, diagnostic and therapeutic procedures in canines can be performed under the state of tranquilization or sedation (Lemke, 2007 and Kushwaha *et al.*, 2012); but major surgical interventions must be performed under general anaesthesia (Rauser and Lexmaulova, 2002; Riazuddin *et al*., 2004 and Hemming, 2010). Surgical management of canine patients, being a painful and inflammatory response, always necessitate an ideal anesthetic, which produces sleep, amnesia, analgesia and muscle relaxation to facilitate well-being of the surgical patient (Vedpathak *et al.*, 2009). Inability of a sole agent to achieve aforementioned characteristics, a combination of drugs is used, which is referred to as balanced anaesthesia (Thurmon and Short, 2007).

In balanced anaesthesia small quantities of more than one drug are used so that the undesirable effects of large quantities of one or two drugs do not create any undesirable clinical effect (Ilkiw, 1999). In balanced anaesthesia multiple drugs include injectable anaesthetic agents which can be used either as total intravenous anaesthesia or to induce anaesthesia prior to maintenance with an inhalant. The total intravenous anaesthesia is associated with prolonged recovery and recumbency time. These disadvantages can be overcome by administration of injectable anaesthetics for induction and maintenance with inhalant anaesthetics (Singh *et al*., 2012). Surgical interventions in animals requiring general anesthesia are routinely maintained via inhalation of volatile anesthetic agents (Seliskar *et al.*,2005 and Trbolova, 2006).

Total Intra Venous Anesthesia (TIVA) involves the use of drugs given solely by repeated or continuous intravenous injection for induction and maintenance of anesthesia (Murrell *et al.,* 2007) but it requires administration of multiple boluses of anaesthetic drugs to maintain adequate level of anaesthesia which result in to

prolonged recovery and several toxic effects to the body. In veterinary practice, intravenous anesthetic drugs are commonly used as induction agents to facilitate endotracheal intubation, whilst inhalation anaesthetic agents used for maintenance of general anaesthesia (Reid, 1996 and McKenzi, 2008). Inhalant anaesthesia is considered safe for maintenance in long and risky procedures as it provides control on depth of anaesthesia, facilitates rapid recovery and is less toxic to the patients when compared with injectable anaesthetic agents (Pottie *et al*., 2008 and Singh *et al*., 2013).

Preanaesthetic medication is an essential component of balanced anaesthesia to facilitate restraining of animal for smooth induction, to increase the duration of surgical anaesthesia and to help in smooth recovery from anaesthesia. A good preanaesthetic sedation facilitates smooth induction and has been shown to have a sparing effect on the induction as well as maintenance dose of intravenous anaesthetic (McCulloch *et al.,* 1992; Muir and Gdawski, 1998 and Laredo, 2015). Premedication is often carried out in small animal practice to calm the animal prior to induction of anesthesia. This sometimes sufficiently allows a procedure such as intravenous catheterization to be carried out. Also, this has been reported to reduce fear and anxiety and contributing to balanced anesthetic technique by providing extra analgesia, counteracting the side effects of other anesthetic drugs, and contributing to a smooth and quiet recovery (Murrell *et al.*, 2007 and Rankin, 2015). In canine practice different levels of sedation and analgesia may be obtained by the use of a number of drugs, including alpha-2 agonists (Ahmad *et al.,* 2013).

Butorphanol has a pharmacological profile exemplary of the agonist-antagonist opioids with multiple actions through the opioid receptor system that are probably mu, delta, and kappa mediated (Horan and Ho, 1989 and Baumann *et al.*,2014). It is used in dogs and cats for analgesia and sedation in combinations with alpha 2 adrenergic agonist (Marini *et al.,* 1992). It is mainly used as a preoperative or postoperative analgesic (Orsini, 1988 and Hosgood, 1990).

Alpha-2 agonists like xylazine, detomidine, dexmedetomidine, romifidine and medetomidine constitute a group of drugs that have been used in veterinary practice for a long time to induce sedation and analgesia. Xylazine and dexmedetomidine, being α2-adrenergic receptor agonists, mediate sedative, anxiolytic and analgesic effects (Clark *et al.*, 2014 and Hopster *et al.,* 2014). Although alpha 2 adrenergic agonist have been used in veterinary anaesthesia since the late 1960s, the

development of dexmedetomidine in the 1990s has led to a renewed interest in the perioperative use of the alpha 2 adrenergic agonist in human (Paris and Tonner, 2005).

Xylazine hydrochloride is a typical alpha-2 agonist of the non-opioid group, having analgesic, sedative and muscle relaxant effects (Wixson *et al.,* 1987). Xylazine was the first alpha 2-adrenergic agonist to be used as a sedative and analgesic in veterinary practice. Its sedative and analgesic activities are related to CNS depression mediated by stimulation of α2-adrenergic receptors (Hsu and Hembrough, 1985). Xylazine is frequently used as sole agents to sedate the animals or combined with opioids to produce different levels of sedation and analgesia. These agents attenuate the stress response to anaesthesia and surgery; reduce anaesthetic and opioids requirements and produce good sedation and analgesia (Gertler *et al.,* 2001). Sedative doses of xylazine cause heart rate and cardiac output to decrease significantly in dogs, while blood pressure and peripheral vascular resistance initially increase, followed by a longer lasting hypotension (Klide *et al.,* 1976; Muir and Piper, 1977 and Ilback and Stalhandske, 2003). Emesis may occur in dogs and cats after xylazine administration either by IM or SC route, which may be caused by activation of central α2 receptors (Lemke, 2007).

Among alpha-2 agonists, dexmedetomidine, an active optical isomer of medetomidine (MacMillan *et al.,* 1996), with sympatholytic, sedative, amnestic and analgesic properties have been described as a useful and safe adjunct in many clinical applications (Mate and Aher, 2019). Dexmedetomidine have higher selectivity towards adrenergic receptors than xylazine (Sinclair, 2003; Lamont *et al.,* 2012 and Quiros-Carmona *et al.,* 2017). Dexmedetomidine is easily reversed with atipamezole, an alpha 2- adrenergic receptors antagonist. It has multifaceted beneficial actions such as sedative, analgesic and anxiolytic properties which has been found to reduce anaesthetic drug requirements in the intraoperative period (Ghodki *et al.,* 2012). It provides sedation with minimal respiratory depression (Kamibayashi and Maze, 2000). Opioids are combined with α2-adrenoceptor agonist to have synergistic action which provide profound sedation and potent analgesia prior to propofol anaesthesia in dog (Salmenpera *et al.,* 1994; Amarpal *et al.,* 1996 and Bol *et al.,* 2000).

Propofol (2,6-di-isopropylphenol compound) is an intravenous (IV) anesthetic used for the induction of general anesthesia (Hall and Chambers, 1987). It is formulated in an aqueous oil-in-water emulsion that contains propofol (10 mg/ml),

glycerol, egg lecithin and soybean oil (Glowaski and Wetmore, 1999). Its duration of action is shorter, owing to its rapid metabolism through liver by glucuronide conjugation (Simon *et al.,* 1988). Cardiorespiratory effects of propofol are similar to those associated with barbiturate anaesthesia, including hypotension and apnoea; pain on injection and postinduction cyanosis are less frequently observed side effects (Smith *et al.,* 1993). Premedication makes it possible to reduce the dose of propofol required to induce anaesthesia (Morgan and Legge, 1989; Weaver and Raptopoulos, 1990 and Geel, 1991) and reduces, but does not eliminate, the incidence of adverse cardiopulmonary and other effects (Smith *at al.,* 1993). Propofol as single agent for total intravenous anaesthesia is generally unsatisfactory due to its poor analgesic property.

The inhalation agents are widely used in veterinary medicine and the main advantages are their elimination independent of the hepatic and renal systems, reduced biotransformation, in addition to low rate of morbidity and mortality compare to other anaesthetic drugs (Tranqulli *et al.,* 2007). Isoflurane is a clear nonflammable, halogenated methyl ethyl ether with a blood gas partition coefficient of 1.46 and is a commonly used inhalant general anaesthetic which has short induction and recovery times with less myocardial depressant properties (Merin *et al.,* 1991; Stoelting, 1999; McEwen *et al*., 2000 and Steffey and Mama, 2007). Isoflurane has many positive characteristics such as low biodegradability, fast onset of action and rapid recovery because of its relatively low blood solubility however; it depresses cardiovascular, pulmonary and neuronal functions in a dose-dependent manner as like other inhalant anaesthetic agents (Steffey and Howland, 1978). Isoflurane, introduced into commercial use since 1970's has been significantly less soluble in blood (Hubbell *et al.,* 1984), have no hepatic side effects and significantly less arrhythmogenic as compared to halothane in dogs and cats (Topal *et al*., 2003 and Altug *et al*., 2009).

Objectives:

1. To assess the sedative effect of xylazine and dexmedetomidine with butorphanol.
2. To study the dose-sparing effect of butorphanol-xylazine/dexmedetomidine combination on propofol.
3. To evaluate and compare clinico-physiological and haemato-biochemical parameters of both the anaesthetic protocols.

CHAPTER 2

REVIEW OF LITERATURE

2.1 BUTORPHANOL

Butorphanol tartrate [17-(cyclobutylmethyl) morphi-nan- 3, 14-diol tartrate], a narcotic agonist-antagonist analgesic, is available for use in humans and dogs (Caruso *et al.,* 1979). Butorphanol tartrate is a synthetic morphinan possessing properties common to opiate analgesics (Meperidine, morphine and oxymorphone), but having some antagonistic properties resulting in its classification as an agonist-antagonist similar to pentazocine and nalbuphine.

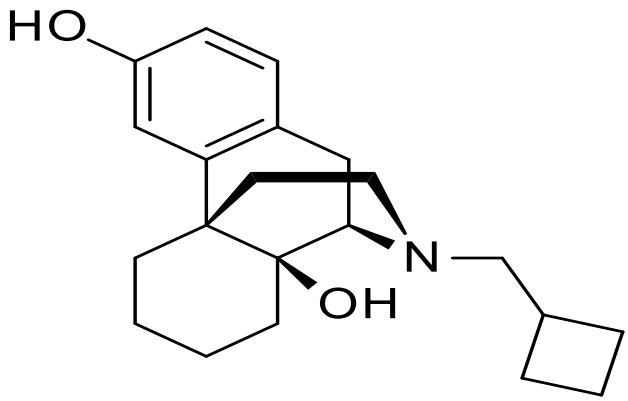

Fig 2.1 Chemical structure of butorphanol

Butorphanol tartrate is an agonist antagonist opioid that exhibits agonist effects at κ (kappa) receptor and antagonist effects at μ (mu) receptors with an analgesic potency 3 to 5 times that of morphine (Lemke, 1999), 20 times than pentazocine, 40 times than meperidine and 50 times less potent than naloxone (Evans *et al.,* 1985). Opioids are traditionally included in balanced anaesthetic protocols for their analgesic property, but they also have sedative effects (Lemke, 2007). Butorphanol is used in cats and dogs for analgesia and sedative in combinations with α-2 adrenoceptor agonists (Marini *et al.,* 1992). Butorphanol produces mild sedation when used alone and analgesia inferior to that of the full μ agonists. Therefore, it is best reserved for minor elective surgical and diagnostic procedures (Kerr, 2016).

Butorphanol has ceiling effect on the degree of analgesia provided and the amount of respiratory depression induced (Pachter and Evens, 1985 and Lascelles, 2000).

Butorphanol may be chosen as a premedication in ASA 1 and 2 patients with preoperative pain or for procedures associated with significant pain intraoperatively

and postoperatively. Its antitussive properties make it a suitable premedication for the brachycephalic patient, enabling longer acceptance of an endotracheal tube in recovery (Dyson, 1990).

Butorphanol is rapidly absorbed after intramuscular administration (Pfeffer *et al.,* 1980) producing sedation with an onset time of less than 15 minutes (Gomes *et al.,*2018). These medications may be used alone or in combination. Butorphanol is frequently combined with α-2adrenoceptor agonist to enhance the level of sedation and both level and duration of analgesia (Hayashi *et al.,*1994; Pypendop and Verstegen, 1994; Ko *et al.,* 2000 and Kuo and Keegan, 2004). The advantages of these combinations are either to improve the results of the combination over either drug as a sole medication or to reduce the incidence of side effects. They are frequently used in young healthy dogs, but with dosage adjustment, it may be safely used in older dogs (Muir *et al.,* 1999).

Butorphanol had marked dose sparing effects on both induction and maintenance agents of anaesthesia (Vijay *et al.,* 2018). Butorphanol as preanaesthetic drug enabled to use a low induction dose of propofol (Sano *et al.,* 2003) and a low concentration of isoflurane for maintenance of general anaesthesia (Mutoh *et al.,* 2002).

Butorphanol facilitated the fastest sedation, indicating that butorphanol may have a superior and more immediate synergistic effect when used with α-2 agonists (Grimm *et al.,* 2000).

Carter and Mercer, (1988) stated that butorphanol produced less respiratory depression and decrease in heart rate than morphine. However; reduction in blood pressure and a transient fall in cardiac output occur in combination with an inhalant anesthetic and therefore the concentration of inhalant anaesthetic should be adjusted to maintain cardiovascular stability (Dyson, 1990).

2.1.1 Clinico-Physiological Effects

Sederberg *et al*. (1981) reported significant decrease in the heart rate, mean arterial pressure, cardiac index and arterial partial pressure of oxygen and minor increase in the systemic vascular resistance index after administration of butorphanol alone.

Ko *et al.* (2000) evaluated the effect of butorphanol on the Minimal Alveolar Concentration (MAC) of isoflurane in dogs. They stated that administration of butorphanol significantly reduces the MAC of isoflurane in dogs. They also reported

reduction in heart rate after butorphanol administration however; blood pressure and SpO_2remain unchanged.

Kuo and Keegan (2004) reported that intravenous administration of butorphanol @ 0.2mg/kg and medetomidine @ 20 µg/kg caused a marked decrease in respiratory rate and respiration rate cardiac output. increases in systolic arterial pressure, mean arterial pressure, diastolic arterial pressure and rectal temperature.

Carpenter *et al*. (2005) stated that butorphanol induces dose dependent sedation and analgesic effect with minimal cardiopulmonary depression which is accompanied by small decrease in arterial blood pressure, heart rate and respiration rate in dogs.

Surbhi *et al.* (2010) studied physiological and biochemical effects of medetomidine-butorphanol-propofol anaesthesia in dogs undergoing orthopaedic surgery. They reported that administration of medetomidine and butorphanol nonsignificantly decreased heart rate and respiration rate whereas; propofol caused tachycardia, decrease in respiration rate and SpO_2. They also observed significant increase in mean arterial pressure after the administration of preanaesthetics, however, hypotension was observed after propofol administration.

Cardoso *et al.* (2014) studied that the administration of the opioids did not further cause bradycardia induced by the dexmedetomidine.

Salla *et al*. (2014) compared the cardiopulmonary effects of intravenous and intramuscular medetomidine and butorphanol in dogs and noticed significant decrease in temperature, systolic, diastolic and mean arterial blood pressure and saturation percentage of oxygen after premedication with medetomidine-butorphanol however; there were no differences in respiration rate.

Rafee *et al*. (2015) observed the effect of dexmedetomidine (D) and dexmedetomidine with butorphanol (DB), as adjunct to midazolam and ketamine anaesthesia, on the clinico-physiological and haemodynamic stability in midazolam and ketamine anaesthesia. Excellent jaw tone relaxation, abolished palpebral reflex with no significant ($P>0.05$) difference between two groups (D and DB) was observed. Heart rate showed an initial increase followed by a decrease, while respiratory rate decreased below the baseline in all the groups. Rectal temperature decreased significantly ($P<0.05$) below the baseline. SBP, DBP and MAP increased initially in both the groups and then decreased until 120 min interval. They concluded

that addition of butorphanol did not have significant effects on the clinico-physiological and haemodynamic stability.

2.1.2 Haemato-Biochemical Effects

Ahmad (2009) reported decrease in haemoglobin and packed cell volume after administration of butorphanol in dogs.

Surbhi *et al.* (2010) reported significant high base values of glucose and cortisol which further increased significantly ($P<0.05$) after the administration of butorphanol and medetomidine. They also reported decrease in plasma urea nitrogen whereas creatinine values increased nonsignificantly ($P>0.05$).

2.2 DEXMEDETOMIDINE

Dexmedetomidine, the latest α-2 agonist, is an active optical isomer of racemate medetomidine, which is used as a sedative and preanaesthetic in veterinary practice. Studies have shown that dexmedetomidine may offer additional sedative and analgesic benefits over medetomidine. In dogs, dexmedetomidine produces dose dependent sedation and analgesia and the intensity of these effects is similar to that produced by twice the dose of medetomidine (Kuusela *et al*., 2000).

Dexmedetomidine is a sedative from α-2 agonist class of drugs with a molecular weight of 236.7 and chemical name (+) -4- [1-(2, 3-dimethylphenyl) ethyl]-1H-imidazole. In the racemic mixture of parent compound medetomidine, dexmedetomidine is the active optical enantiomer and displays specific and selective alpha-2 receptor agonism; whereas levomedetomodine is considered to be pharmacologically inactive. Dexmedetomidine hydrochloride is a white to almost white powder that is freely soluble in water and has a pKa of 7.1 (Abbott lab, 2000). Dexmedetomidine is the first isomer specific drug to be licensed in animals and represents a jump forward in the development and use of stereospecific agents instead of the use of nonspecific racemic mixtures.

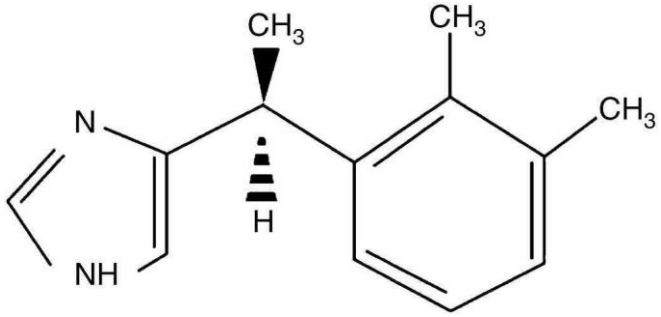

Fig 2.2 Chemical structure of Dexmedetomidine

Dexmedetomidine is used in both human and veterinary medicine. In human medicine it is used as a short-term medication (<24 hr) for analgesia and sedation in the intensive care units (Shukry and Miller, 2010). The major applications in human medicine include premedication, anaesthetic adjunct to the regional and general anaesthesia and as postoperative sedative and analgesic; similar to benzodiazepines but it appears to have more beneficial effects (Gertler *et al.*, 2001). In veterinary practice it is used for premedication and as an adjunct to general anaesthesia in several species (Kuusela *et al.*, 2001, Kutter, 2006; Sano *et al.*, 2010; Ahmad *et al.*, 2013 and Santosh *et al*., 2013).

Alpha-2 agonists exert their effects through the action on alpha-2 adrenergic receptors. Like other α-2 agonists, dexmedetomidine acts on the presynaptic α-2 receptors on various neuronal and non-neuronal sites and inhibits the release of noradrenaline from sympathetic nerve terminals. Dexmedetomidine mediated activation of the α-2 adrenergic receptor results in activation of G-proteins, which modulate cellular activity by signaling a second messenger system, leading to the inhibition of adenylate cyclase which in turn results in decreased formation of 3, 5-cyclic adenosine monophosphate (cAMP) (Birnbaumer *et al*., 1990 and Cotecchia *et al*., 1990). All these events result in efflux of K+ through an activated channel causing hyperpolarization and suppression of neuronal firing. Entry of Ca++ into the nerve terminals is also reduced by α-2 adrenoceptor activation, which may be responsible for its inhibitory effects on secretion of neurotransmitters (Hayashi *et al*., 1995 and Khan *et al*., 1999).

Co-administration of alpha-2 adrenoceptor agonists with opioids or benzodiazepines may result in pronounced sedation and analgesia (Muir, 1998). Administration of dexmedetomidine with butorphanol resulted in greater sedative effect, greater muscle relaxation and increased auditory response scores, compared with administration of dexmedetomidine alone (Selmi *et al.,* 2003).

Dexmedetomidine is a potent sedative and analgesic, and confers good muscle relaxation but its use is characterized by marked cardiovascular effects, classically described as an increase in systemic vascular resistance (SVR), decreased heart rate and cardiac index and increased central venous pressure (Bloor *et al.*, 1992). Dexmedetomidine is the dextro-rotatory isomer of medetomidine and may have some advantages over the racemate in terms of increased analgesic potency (Kuusela *et al.* 2000). Dexmedetomidine causes marked bradycardia; this may be less than observed

with medetomidine. Analgesic effects of dexmedetomidine are dose dependent; and are present at IV doses as low as 2 µg/kg (Kuusela *et al.* 2001).

2.2.1 Clinico-Physiological Effects

Bloor *et al.* (1992) studied hemodynamic and sedative effects of a single dose of dexmedetomidine (20 µg/kg) in isoflurane-anesthetized dogs. They reported 67% increase in arterial pressure with concomitant decrease in heart rate by 53% and cardiac output by 74%. Arterial blood pressure remains at least 20% above the baseline, while heart rate was 40% lower than baseline throughout the study. They also reported that dexmedetomidine administration reduced isoflurane anesthetic requirements by 89% at 30 min and by 50% at 4 hr.

Kuusela *et al.* (2000) reported significantly decline in heart rate within five minutes after intravenous administration of dexmedetomidine at the dose rate of 10 and 20µg/kg. The decrease in heart rate after dexmedetomidine administration might be due to reflex bradycardia as a result of alpha-2 agonist-induced vasoconstriction (Lemke, 2007).

Kuusela *et al.* (2000) compared the clinical effect and pharmacokinetics of medetomidine and its enantiomer, dexmedetomidine and levomedetomodine in dogs. Sedative effects of med40, dex20, and dex10 and overall level of sedation did not differ between these treatments during the first hour. Heart rate decrease significantly after MED40, DEX20 and DEX10 but after 90 minute it become normal in DEX10. Respiration rate decreases significantly after MED40, DEX20 and DEX10 administration. Systolic and diastolic blood pressure changes nonsignificantly after dexmedetomidine and medetomidine administration.

Gertler *et al.* (2001) observed that the uses of alpha-2 agonist drugs have increased many folds since their discovery. Dexmedetomidine has been ascribed having the property of anaesthetic sparing and haemodynamic stability. It can be beneficial in ischemia. Patients treated with dexmedetomidine suffered some degree of hypotension which had to be corrected medicinally. It gives good quality sedation. It was recommended that it should be given as a constant rate infusion and not as a bolus.

Kuusela *et al.* (2001) reported that the reduced requirement for propofol with dexmedetomidine and medetomidine. Seidel *et al.* (1995) reported that This marked reduction is due to central alpha-2 receptor agonism in the locus coeruleus, causing sedation, hypnosis and marked synergy with GABA minergic anaesthetic agents.

Gomez-villamandos *et al.* (2006) evaluated dexmedetomidine as a premedicant in dogs prior to propofol–desflurane anaesthesia. They reported that heart rate and respiration rate decreased significantly during dexmedetomidine sedation. A progressive decrease in MAP, SAP and DAP was observed in all groups but no statistical differences were found between the sedative groups. They concluded that the combination of dexmedetomidine, propofol and desflurane appears to be effective for induction and maintenance of general anaesthesia in healthy dogs.

Granholm *et al.* (2007) investigate sedative, analgesic and cardiorespiratory parameter after intramuscular and intravenous administration of medetomidine and dexmedetomidine in 212 dogs. They stated that the dogs have shown clear dose-dependent sedative analgesic effects above the baseline values by 5 minutes after administration of dexmedetomidine and medetomidine and were higher for intravenous route than intramuscular route. They found marked decrease in heart rate, respiratory rate and body temperature of the dogs treated either intravenous or intramuscularly. Peak sedative and analgesic effects were observed between 15 - 30 minutes after intravenous and 30 minutes after intramuscular doses.

Lemke (2007) stated a drop in rectal temperature following dexmedetomidine administration which may be attributable to a decrease in heat output due to sedation and reduced muscle activity. Hypothermia may have been exacerbated by the activation of α-2 C receptors.

Surbhi *et al*. (2010) opined that α-2 agonist reduces the packed cell volume and hemoglobin values which may be due to pooling of circulating erythrocytes in the spleen or other reservoirs secondary to reduced sympathetic stimulation.

Bell *et al.* (2011) assessed sedative, cardiopulmonary and propofol sparing effects of dexmedetomidine and buprenorphine compared to acepromazine and buprenorphine in dogs. Dogs receive 15 µg/kg buprenorphine combined with either 30 µg/kg acepromazine (group 1), 62.5 µg/m^2 dexmedetomidine (group 2) or 125 µg/m^2 dexmedetomidine (group 3) intramuscularly. After 30 minutes, anaesthesia was induced using a propofol target controlled infusion. They do not observe significant differences in sedation or quality of induction between the groups. Heart rate was significantly lower and arterial blood pressures higher in dexmedetomidine groups than other groups, but there was no significant difference between dexmedetomidine groups. Propofol targets were significantly lower in dexmedetomidine groups. He

concluded that both doses of dexmedetomidine produced characteristic cardiovascular and respiratory effects of a similar magnitude.

Congdon *et al*. (2011) studied the sedative and cardiovascular effects of intramuscular administration of dexmedetomidine with and without concurrent atropine administration in dogs. They reported that administration of atropine at 0.02 mg/kg, IM with dexmedetomidine at 10μg/kg IM resulted in an increase in mean arterial blood pressure and heart rate; deleterious cardiac arrhythmias were also observed. The findings suggested that there was no benefit to the use of atropine to treat dexmedetomidine induced bradycardia. Heart rate might increase or prevent the dexmedetomidine induced bradycardia, but no increase in cardiac output was observed with the concurrent use of atropine with dexmedetomidine.

Krimins *et al.* (2012) studied effects of dexmedetomidine on anesthetic, analgesic and cardiopulmonary variables in dogs with butorphanol–zolatile (DBTZ) or tramadol-ketamine (DtrK) combinations. Duration of analgesia was significantly longer with DBTZ treatment (60-70 min), compared with that of DTrK treatment (40-50 min). They reported significant decrease in heart rate from baseline values 5 minutes after injection, which subsequently return to normal from 10-20 minutes after injection however; mean arterial pressure increase significantly compared with base line value. Rectal temperature remains in normal range.

Lervik *et al.* (2012) studied continuous rate infusion of dexmedetomidine in which anaesthesia was induce using propofol and maintain by isoflurane. They concluded that dexmedetomidine causes significant decrease in heart rate, increased blood pressure and in some instances caused second degree atrioventricular block, but all parameters remained within clinically acceptable limits for healthy dogs.

Ahmad *et al.* (2013) used dexmedetomidine alone and in combination with midazolam, fentanyl and ketamine. They observed decrease in heart rate and respiration rate whereas, mean arterial pressure increased first and then decreased. Rectal temperature was non- significantly increased initially followed by decrease to base values. Pedal and palpebral reflexes had the greatest score for groups in which dexmedetomidine used in combination rather than alone. They concluded that dexmedetomidine can be used alone or in combination of the above drugs to achieve sedation or complete anaesthesia as desired. They reported that in order to achieve good sedation, it is better to use a combination of drug than any single drug due to the phenomenon of synergism which reduces the dose of individual drugs.

Congdon *et al.* (2013) have investigated the impacts of dexmedetomidine on cardiovascular, respiratory and acid base balance in dogs which were induced with propofol and maintained on isoflurane. They reported non-significant difference in the respiration rate, body temperature, heart rate, mean arterial pressure, systolic arterial pressure and diastolic arterial pressure than baseline values however; plasma glucose increased after administration of dexmedetomidine.

Santosh *et al.* (2013) evaluated midazolam-ketamine with dexmedetomidine and fentanyl for general anaesthesia in dogs. The animals received 0.4 mg/kg midazolam and 10 µg/kg dexmedetomidine (group A), 0.4 mg/kg midazolam and 20 µg/kg dexmedetomidine (group B) and 0.4 mg/kg midazolam + 20 µg/kg dexmedetomidine + 4 µg/kg fentanyl (group C) intramuscularly, using separate syringes. Ten minutes later Ketamine was administered intravenously in all the groups. Pedal reflex was abolished up to 30 min in dexmedetomidine groups. Respiratory rate decreased significantly throughout the observation period, but rectal temperature decreased significantly towards the end of the observation period in all the groups. Heart rate decreased significantly in the animals of group B. Mean arterial pressure was maintained within the physiological range in all the groups. It was concluded that dexmedetomidine (10 µg/kg)-midazolam-ketamine can produce anaesthesia for about 20 min in dogs. Increasing the dose of dexmedetomidine did not enhance the duration of anaesthesia.

Cardoso *et al.* (2014) evaluated the cardiorespiratory, sedative effects of dexmedetomidine alone or in combination with methadone, morphine or tramadol in dogs. They observed decrease in heart rate, respiration rate, rectal temperature and systolic blood pressure after opioids and dexmedetomidine anaesthesia. They concluded that the administration of opioids with dexmedetomidine produces similar effects on the HR, SAP, respiration rate and RT compared with the use of dexmedetomidine alone in dogs. The combinations with opioids appeared to provide deeper sedation.

Jena *et al.* (2014) studied clinical evaluation of total intravenous anaesthesia using xylazine or dexmedetomidine with propofol in dogs. They reported heart rate decrease significantly ($p<0.01$) from 10 min up to 15 min in dexmedetomidine group. Respiration decreased significantly at 10 min and values remained significantly ($p<0.01$) lower than the base value. There was a slight and non-significant ($p>0.05$) increase in RT at 5 min, 10 min, which is followed by a significant ($p<0.01$) decline

in RT from 15 min onwards in dexmedetomidine group. In dexmedetomidine group there was non-significant ($p>0.05$) increase in SBP at 10 min time interval. SpO_2 remained almost similar or slightly increased non-significantly at different time intervals.

Sharma *et al.* (2014) used atropine-butorphanol-xylazine-ketamine and atropine-butorphanol-dexmedetomidine-ketamine combination for induction of anaesthesia and maintained on halothane. They reported high score in pedal and palpebral reflexes throughout the study. They did not observe any significant change in haemato-biochemical parameters in dexmedetomidine group. They observed better quality of recovery and significantly less recovery time in dexmedetomidine group than xylazine group.

Diao *et al.* (2015) compared respective effects of propofol and emulsified isoflurane administered alone and in combination with dexmedetomidine on the quality of induction of anesthesia, physiological variables and recovery in dogs. They reported that pulse rate and respiration rate decreased significantly after dexmedetomidine-propofol administration. SpO_2 decreased non-significantly after dexmedetomidine-propofol anaesthesia.

Grasso *et al.* (2015) evaluated hemodynamic influence of acepromazine or dexmedetomidine premedication in dogs anaesthetized with propofol and maintained on isoflurane. They stated that dexmedetomidine reduced cardiac output but prevented propofol-isoflurane induced hypotension. They also reported that oxygen carrying capacity and PCV were higher in dexmedetomidine treated dogs than in acepromazine treated dogs.

Kellihan *et al.* (2015) evaluated the echocardiographic variables and sedation after two dosages of dexmedetomidine combined with butorphanol in healthy dogs. In group I dexmedetomidine @ 5 mcg/kg IM and butorphanol @ 0.4 mg/kg and in group II dexmedetomidine @ 10 mcg/kg IM and butorphanol @ 0.4 mg/kg were administered. They found significant decrease in heart rate and respiration rate in both the groups after dexmedetomidine administration but there was no significant change in rectal temperature. There were no significant changes in systolic blood pressure, diastolic blood pressure and mean arterial blood pressure during all point of time in group I where as systolic and mean blood pressure was lower in group II. They observed significantly higher sedation score in group II. They concluded that There were significant hemodynamic changes, mainly related to HR and indices of systolic function, following administration of dexmedetomidine in dogs.

Mazumdar *et al.* (2015) evaluated the effect of dexmedetomidine @ 20 µg/kg body weight and @ 40 µg/kg body intramuscularly in dogs and found reduction in haemoglobin, packed cell volume, total erythrocyte count and total leukocyte count. There was significant increase in blood glucose, blood urea nitrogen (BUN) and creatinine level in the dogs of both the groups. There was non-significant decrease in total protein level in the dogs of both the groups.

Rauser *et al.* (2016) reported significant decrease in heart rate and respiration rate in dexmedetomidine-propofol-isoflurane anaesthesia however; no significant changes in systolic arterial pressure (SAP), diastolic arterial pressure (DAP) and SpO_2 was also observed.

Yadav *et al.* (2016) compared suitability and efficacy of three preanaesthetic combinations administered intramuscularly *viz.*, glycopyrrolate (0.01 mg/kg) + xylazine (0.5 mg/kg) + butorphanol (0.2 mg/kg) in group I; glycopyrrolate (0.01 mg/kg) + dexmedetomidine (5 mcg/kg) + butorphanol (0.2 mg/kg) in group II; glycopyrrolate (0.01 mg/kg) + acepromazine (0.05 mg/kg) + butorphanol (0.2 mg/kg) in group III for propofol-halothane anaesthesia in clinical cases of dogs. The preanaesthetic combinations in all three groups produced mild to moderate sedation in the animals and decreased the requirement of propofol for anaesthetic induction. Clinico-physiological parameters in animals of all groups altered within physiological limit and reach to near normal value at recovery. Preanaesthetic combination of glycopyrrolate (0.01 mg/kg) + dexmedetomidine (5 mcg/kg) + butorphanol (0.2 mg/kg) was found to be the best among three combinations in terms of the quality of sedation, early onset of sedation and dose sparing effect on induction and maintenance agents.

Arunkumar *et al.* (2017) evaluated clinical and physiological effects of dexmedetomidine, xylazine and triflupromazine as preanaesthetics with propofol-isoflurane anaesthesia for various surgeries in dogs. The rectal temperature decreased non-significantly in dexmedetomidine treated dogs, except at 10min where non-significant increase in rectal temperature observed. Respiratory rate decreased significantly ($P \leq 0.01$) till the end of study period in dexmedetomidine group. Heart rate decreased non-significantly till the end of study period in dexmedetomidine, except at 10 minutes interval and 5 minutes after induction where it was increased significantly and increase non-significantly respectively.

Micieli *et al.* (2017) compared the clinical effects and sedation scores following either intranasal or intramuscular administration of dexmedetomidine in dogs. They found higher sedation score in the intranasal group as compared to the intramuscular group. At the time of peak sedation, heart rate decreased to 56% from baseline values in the intramuscular group and 18% in the intranasal group. No significant differences in SpO_2 were found between the two groups at any point of time. No significant changes in mean arterial pressure after IM administration. They reported decrease in respiration rate shortly after dexmedetomidine administration. They concluded that intranasal dexmedetomidine @ 0.02 mg/kg produced more profound sedation than intramuscular administration in healthy dogs and may be considered as an alternative route for dexmedetomidine administration in dogs.

Kumar *et al.* (2018) compared clinico-physiological, and haemodynamic effects of propofol and ketamine anaesthesia with dexmedetomidine-butorphanol premedication in goats. They observed gradual decrease in heart rate which remains significantly lower than the baseline value in both groups until the end of the observation period. Respiratory rate decreased significantly after premedication. The respiration rate continued to decrease significantly lower than the baseline after induction of anaesthesia in butorphanol-dexmedetomidine-propofol up to 45 min. Rectal temperature decreased non-significantly after premedication with dexmedetomidine and butorphanol. Mean arterial pressure (MAP) decreased significantly after premedication and induction of anaesthesia in both groups.

Nishimura *et al.* (2018) evaluated cardiopulmonary, sedative, and antinociceptive effects of dexmedetomidine combined with butorphanol, meperidine and morphine in dogs. Heart rate was reduced at all time points after injection of dexmedetomidine with opioids. There was a significant reduction of mean arterial blood pressure for dexmedetomidine with butorphanol, meperidine and morphine, compared with baseline. There was a significant decrease in respiratory rate, compared with the baseline value, for dexmedetomidine and dexmedetomidine combined with opioids. They stated that the sedative effects of dexmedetomidine were more pronounced when it was combined with a variety of opioids, particularly with butorphanol, meperidine, and methadone, compared with the sedative effects when dexmedetomidine was administered alone to healthy dogs. They concluded that dexmedetomidine combine with opioids cause similar cardiorespiratory depression as

dexmedetomidine alone however; better sedation was achieved when dexmedetomidine combined with opioids.

Sahoo *et al.* (2018) compared sedative effect of dexmedetomidine/ xylazine in combination with butorphanol-midazolam as preanaesthetic to ketamine anaesthesia for ovariohysterectomy in dogs. They reported adequate muscle relaxation, sedation and analgesia along with smooth and uneventful recovery after dexmedetomidine. Onset of sedation and induction time was quicker in dexmedetomidine group. Pedal reflex, palpebral reflex, jaw tone and muscle relaxation were mild after dexmedetomidine and xylazine administration. Rectal temperature, heart rate and respiration rate decrease non-significantly from base value after dexmedetomidine administration. They concluded that onset of sedation, induction of anaesthesia and recovery were quicker and smoother with administration of dexmedetomidine providing better degree of basal anaesthesia than xylazine.

Vijay *et al.* (2018) evaluated butorphanol and fentanyl in preanaesthetic protocols to dexmedetomidine-propofol-isoflurane anaesthesia in adult and geriatric canine patients. A significant decrease in HR was observed after 5 min of administration of preanaesthetics with a subsequent increase from 10/15 min intervals. Significant decrease in respiratory rate was seen after administration of preanaesthetics till recovery from anaesthesia. Significant fall in rectal temperature was recorded between 5 and 10 min of anaesthesia in all the animals. SpO_2 showed increasing trend from 5 min up to the end of the observation period. MAP increased non significantly after 5 min of preanaesthetic administration in animals of glycopyrrolate-dexmedetomidine-butorphanol. They concluded that preanaesthetic combination of glycopyrrolate-dexmedetomidine-butorphanol was better in comparison to glycopyrrolate-dexmedetomidine-fentanyl in terms of the sedation quality, recovery time, dose sparing action on the induction and maintenance agents used and better maintenance of the cardiopulmonary dynamics and haemodynamics in both adult healthy and geriatric canine patients.

Aslam *et al.* (2019) studied clinico-biochemical effects of different pre anesthetic drugs combined with propofol for neutering dogs. In which xylazine 2.2 mg/kg, diazepam 0.25 mg/kg and medetomidine 40 µg/kg body weight, were injected intramuscular as preanaesthetics in A, B and C groups. After 3-5 minutes of preanesthetic, the propofol injection @ 6 mg/kg of body weight was administered intravenous as anesthetic drug in all three groups. A non-significant reduction was

observed in rectal temperature in medetomidine group. Pulse rate initially decrease in medetomidine treated groups due to peripheral vasoconstriction followed by vasodilatation. Respiratory rate depression was observed in medetomidine group due to direct depression of respiratory centre in central nervous system.

Mate and Aher (2019) evaluated clinic-physiological changes after intravenous administration of dexmedetomidine-butorphanol and dexmedetomidine-midazolam as preanaesthetic with propofol anaesthesia in dog. Evaluation of various reflex revealed profound sedation with excellent jaw relaxation, moderate to completely abolished palpebral and pedal reflex and rostroventral eyeball position making pupil invisible during and anaesthesia. Heart rate decreases significantly in butorphanol-dexmedetomidine group at 10 mins. Immediately after propofol administration a non-significant increase till 30 min, whereas it was decreased non-significantly at 45 min, thereafter it was increased non-significantly till recovery at which the value returns near to the baseline. Respiration rate decreases significantly in butorphanol-dexmedetomidine group at 10 mins and then significant increase ($P<0.01$) was observed from 30 min till 45 min after propofol administration. Rectal temperature increases non-significant in DB administration till 45 min after propofol administration. They concluded that intravenous administration of dexmedetomidine-butorphanol preanaesthetic combinations produced profound sedation, rapid onset of action and excellent degree and depth of analgesia. Dexmedetomidine- butorphanol along with propofol produces better quality and degree of basal anaesthesia for the minor and major surgeries in canines.

Saini *et al.* (2019) studied clinico-physiological and haemato-biochemical effects of thiopental sodium and ketamine anaesthesia with or without dexmedetomidine premedication in dogs. They reported reduction in dose of thiopental sodium from 15.21±0.31 mg/kg to 6.23±0.18 mg/kg after dexmedetomidine administration. Similarly, preanaesthetic administration of dexmedetomidine reduced the desired dose of ketamine from 10 mg/kg to 3.17±0.15 mg/kg body weight. Based on this study, it was concluded that dexmedetomidine premedication prior to administration of ketamine and thiopental sodium results in quicker induction, better anaesthesia for prolonged duration with better muscle relaxation as compared to use of ketamine and thiopental sodium alone.

2.2.2 Haemato- biochemical effect

Dollery (1991) suggested that Increase in blood glucose level might be attributed to the effect of α-2 adrenoceptor agonists that was associated with growth hormone stimulation and insulin suppression through direct inhibitory effect of dexmedetomidine on the pancreatic β-cells. Surbhi *et al.* (2010) stated that low insulin activity causes inhibition of serum glucose utilization that leads to rise in serum glucose level.

Skarda and Muir (1996) have reported decreased in haemoglobin and pack cell volume after administration of α2-adrenoceptors agent in dogs which occurs due to due to decrease in sympathetic activity after dexmedetomidine administration and it leads to spleenic pooling of circulatory erythrocytes.

Pypendop *et al.* (2011) characterized the hemodynamic effects of dexmedetomidine in isoflurane-anesthetized cats. They stated that heart rate, haemoglobin and oxygen saturation decreased following dexmedetomidine administration. Arterial blood pressure increased following dexmedetomidine administration. packed cell volume, arterial hemoglobin concentration, mixed-venous hemoglobin concentration and glucose concentration increased following dexmedetomidine administration. They concluded that the use of dexmedetomidine as an anesthetic adjunct is expected to produce greater negative hemodynamic effects.

Restitutti *et al.* (2012) suggested that level of plasma glucose increases significantly after dexmedetomidine administration. They reported that fluctuations in creatinine value during dexmedetomidine administration. This was due to the inhibitory effect of drugs on the renal blood flow, which led to increased creatinine production from muscle damage and amino acid degradation.

Guedes and rude (2013) investigate the effect of medetomidine on plasma glucose and insulin in dogs in healthy dogs undergoing anesthesia and surgery. Medetomidine significantly decreased plasma insulin concentrations and increased plasma glucose concentrations in healthy dogs. They concluded that Pre-anesthetic administration of medetomidine significantly suppressed insulin secretion and increased plasma glucose concentration in healthy dogs undergoing anesthesia and surgery.

Umar and Adam (2013) evaluated Effects of Combination of Ketamine-Medetomidine Anaesthesia on haematology and Some Serum Chemistry Parameters in Dogs. They reported significant decreases in PCV, RBC and haemoglobin while

WBC values showed significant increase at 60 minutes compared with base line values (0 min). BUN did not differ significantly compared with base line (0 min). Neutrophils increased as compared to the base line value, lymphocytes showed significant decrease while monocytes and eosinophils did not differ significantly. Alpha 2 agonists premedication in dogs produced transient decrease in PCV, Hb, RBC and lymphocytes and significant increase in WBC, neutrophils and CRE. There was no significant effect on BUN and ALT.

Jena *et al*. (2014) evaluated and compared the clinico-physiological, hemodynamic and hematobiochemical effects in response to different total intravenous anaesthesia techniques using xylazine or dexmedetomidine with propofol in canine patients. They reported significant decrease in Hb and non-significant decrease in PCV from the base value were recorded in dexmedetomidine group at 30 min. Blood glucose was non- significant decline in dexmedetomidine group that remained below the base value. Blood urea nitrogen and creatinine was a non-significant decrease at 30 min followed by a non-significant increase at 60 min. TLC showed a non-significant increase at 30 min followed by non-significant decrease at 60 min in dexmedetomidine-propofol anaesthesia. Neutrophil count showed non-significant increase in both the groups whereas lymphocyte count showed a non-significant decrease in dexmedetomidine group. Eosinophil count showed a non-significant decrease in dexmedetomidine group.

Mazumdar *et al.* (2015) evaluated the effect of dexmedetomidine @ 20 µg/kg body weight and @ 40 µg/kg body intramuscularly in dogs and found reduction in haemoglobin, packed cell volume, total erythrocyte count and total leukocyte count. There was significant increase in blood glucose, blood urea nitrogen (BUN) and creatinine level in the dogs of both the groups. There was non-significant decrease in total protein level in the dogs of both the groups.

Saini *et al.* (2019) Clinico-physiological and haemato-biochemical effects of dexmedetomidine as preanesthetic, thiopental sodium and ketamine as induction in dogs. There was a gradual and nonsignificant decrease in haemoglobin level in all the animals. After dexmedetomidine administration prior to ketamine, PCV level decreased significantly at 60 min. The level of total erythrocytes counts decreases significantly in all the animals. Decrease in haemoglobin (Hb), packed cell volume (PCV), and total erythrocyte count (TEC) in both the groups at various time intervals may be attributed to the pooling of blood cells in the spleen, induced by the

adrenolytic property of alpha 2 adrenoceptor drugs. Total leucocyte count increases non significantly up to 60 min after dexmedetomidine and ketamine anaesthesia. Nonsignificant changes in monocytes, basophils and eosinophils were observed in all animals. Level of glucose increases insignificantly after dexmedetomidine and ketamine anaesthesia. A nonsignificant transient decrease in the level of total protein was observed in all animals. Level of BUN increase nonsignificantly after dexmedetomidine and ketamine anaesthesia. Nonsignificant increase in ALT and AST in all the animals.

2.3 XYLAZINE HYDROCHLORIDE

Xylazine was the first α-2 - agonist to be used by veterinarians. The drug was synthesized in West Germany in 1962 for use as an antihypertensive in people but was found to have potent sedative effects in animals (Grimm *et al.* 2011). The chemical name for xylazine is 2(2,6-dimethylphenylamino)-4H- 5,6-dihydro-l,3-thiazine hydrochloride (Greene and Thurmon, 1988). In 1981, the sedative and analgesic effects of xylazine were definitively linked to activation of central a2-adrenergic receptor agonist. Its sedative and analgesic activities are related to CNS depression mediated by stimulation of α2-adrenergic receptors (Hsu *et al.,* 1985). Xylazine has been used in clinical practice by veterinarians since the late 1960s (Haskell *et al.,* 2003).

Xylazine is used in dogs and cats for short-term sedation and analgesia for diagnostic or minor surgical procedures. Neuroleptanalgesia is achieved when α2-adrenergic receptor agonists are combined with opioids. Xylazine is also given with ketamine for restraint or for brief surgical procedures when injectable anesthesia is preferred. It is useful as a premedication, providing good sedation for IV catheter placement and reduced doses of induction agent (Rankin, 2015).

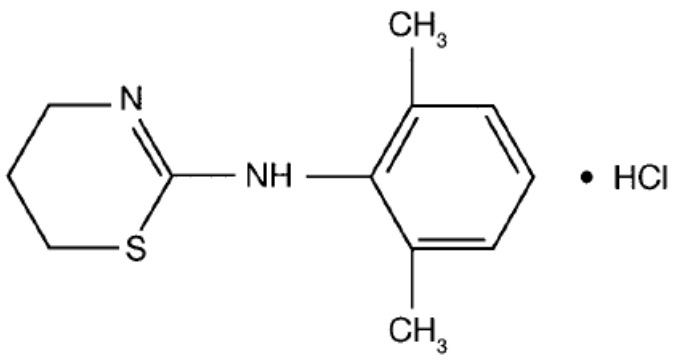

Fig. 2.3 Chemical structure of Xylazine

Xylazine have been used in dogs for sedation and anesthetic premedication (Ilback and Stalhandske, 2003 and Monteiro *et al.,* 2008). The main negative cardiovascular effects of all α_2-agonists include bradycardia and associated arrhythmias ($1^{st}$and 2^{nd} degree atrioventricular heart block), a dramatic reduction in cardiac output by up to 50%, and an increase in systemic vascular resistance (Ilback and Stalhandske, 2003 and Sinclair,2003).

Tranquilli *et al.* (2007) stated that the xylazine can be given IV or IM, but the IM route is preferred over IV route because cardiovascular side effects are reduced. Intramuscular doses for healthy dogs and cats range from 0.5 to 1.0 mg/kg.

Xylazine is widely used as centrally acting α_2-adrenergic receptor agonist with potent sedative, analgesic and muscle relaxant activity (Pandey *et al*., 1996). It is commonly used in canine surgery either alone or in combination with other sedative, analgesic or anaesthetic agents (Booth, 1992).

Xylazine is the shortest acting α 2 –adrenergic agonist and has been widely used as preanaesthetic for immobilizing dogs as well as for sedative, muscle relaxant, and analgesic purposes (Sutil *et al*., 2017). Dogs demonstrated xylazine elimination half-lives of about 30 min after 1.4 mg/kg (Garcia-Villar *et al.,* 1981).

Emesis may occur in dogs and cats after xylazine administration by either the IM or SC route, which may be caused by activation of central α2 receptors (Lemke, 2007).

2.3.1 Clinico-Physiological Effects

Cullen and Reynoldson (1993) studied xylazine or medetomidine premedication before propofol anaesthesia. They reported that bradycardia was a common feature in all the dogs given xylazine or medetomidine, but hypertension was consistently recorded in all the dogs given medetomidine.

Redondo *et al.* (1999) compared xylazine, medetomidine and romifidine as premedicant to propofol and halothane-N_2O anaesthesia. They stated that pulse rate was decrease significantly after xylazine and medetomidine administration. Respiration rate also decreased after xylazine administration. There was no difference observed in RT, MAP, SAP and DAP.

Gleed and Seymour (1999) stated that the onset of action after intramuscular administration of xylazine is approximately 10 to 15 minutes and after intravenous administration is 3 to 5 minutes. Analgesic effects of xylazine last for about 15 to 30

minutes, and sedation may persist for 1 to 2 hours. Complete recovery after xylazine administration may take 2 to 4 hours. They stated that xylazine depresses thermoregulatory mechanisms and either hypothermia or hyperthermia may occur depending upon the ambient temperature.

Ilback and Stalhandske (2003) studied the cardiovascular effects of xylazine recorded with telemetry in the dog. Heart rate decreased for about 10 min and was continuously depressed during 60 min. Both systolic and diastolic blood pressure increased immediately after administration of xylazine. The systolic blood pressure showed a peak increase for about 5–10 min and then decreased below the baseline value. The diastolic blood pressure peaked 5–10 min after xylazine administration but did not return to baseline level until 50 min after administration. Body temperature decreased continuously for about 90 min and remained low for more than 4 h after treatment.

Mukati *et al.* (2006) studied clinico-physiological effects of propofol alone and in combination with xylazine or acepromazine in dogs. They reported that significant increase in pulse and heart rate and non-significant decrease in body temperature in xylazine-propofol anaesthesia. The respiration rate decreased significantly in xylazine-propofol anaesthesia. They concluded that xylazine as premedicant results in prolonged duration of anaesthesia with reduced induction dose of propofol and has more sedative and analgesic and muscle relaxation properties with propofol.

Tranquilli *et al.* (2007) stated that the sinus bradycardia and AV block are the arrhythmias that are encountered most commonly after xylazine administration. Development of these arrhythmias is a normal physiological response to the increase in vagal tone induced by xylazine.

Monteiro *et al.* (2008) evaluated the effects of methadone, administered alone or in combination with acepromazine or xylazine, on sedation and on physiologic parameters in dogs. They reported greater sedation in xylazine and xylazine-methadone. Xylazine produce maximum sedation when use with opioids. They reported that heart rate, rectal temperature and respiration rate decreases significantly after administration of xylazine and xylazine-methadone. Systolic arterial pressure decreases non significantly in xylazine and xylazine-methadone. Sedation was greater in xylazine than other preanaesthetics.

Welsh (2009) stated that xylazine (but apparently not the other alpha 2 adrenergic agonists) will sensitize the heart to catecholamines, with the result that cardiac arrhythmias are not uncommon in xylazine sedated patients and also explained that alpha 2 adrenergic agonists have relatively mild depressant effects on ventilation in dogs and cats. Respiratory rate usually slows and may become intermittent in nature with deep sedation, but arterial blood gas values are fairly well maintained.

Dewangan *et al.* (2010) studied clinico-physiological and cardiopulmonary response to xylazine-propofol anaesthesia in dogs. In which xylazine was administered at 1.0 mg/kg IM, and propofol was administered 10 min later to all the animals @ 4 mg/kg IV. Corneal, palpebral, rectal pinch and pedal reflexes were abolished after xylazine-propofol anaesthesia. The recovery from anaesthesia was smooth, rapid, free from excitement and quiet. They reported significant ($P<0.01$) decrease in heart rate and respiratory rate after xylazine-propofol anaesthesia. They observed non-significant decrease in rectal temperature after xylazine-propofol anaesthesia. They concluded that xylazine-propofol anaesthesia could be safe anaesthetic protocol to use in dogs.

Grimm *et al.* (2011) reported that alpha-2 agonist initially causes vasoconstriction, increased BP, and reflex vagal bradycardia; and later cause decreased sympathetic tone, sympathetically driven HR, and BP. Alpha-2 agonist occasionally causes AV blockade which occurs secondary to the initial increase in BP and reflex (baroreceptor-mediated) increase in vagal tone.

Ko (2013) stated that respiratory depressive effects of alpha 2 adrenoceptor agonists are minimal when the drugs are used alone, but when used in combination with opioids, ketamine, or tiletamine-zolazepam, profound respiratory depression may be induced in dogs and cats.

Cassu *et al.* (2014) investigated the sedative and clinical effects of the pharmacopuncture with xylazine, compared to the conventional dose of intramuscular xylazine injection in dogs. They reported that sedative effect was observed in both groups. The greatest score sedation was observed at 15 and 30 min, respectively in X-IM and X-Yintang groups. They reported marked reduction in the HR and increased incidence of ECG abnormalities in xylazine intramuscular group. In both treatment groups, minimal changes were observed in relation to SABP, RR, RT and blood glucose. They concluded that pharmacopuncture with xylazine induced clinically

relevant sedative effects in dogs, with the advantage of reduction of undesirable side effects associated with α2-agonists, including bradycardia, cardiac arrhythmias, and emesis.

Jena *et al*. (2014) evaluated and compared the clinico-physiological, hemodynamic and hematobiochemical effects in response to different total intravenous anaesthesia techniques using xylazine or dexmedetomidine with propofol in canine patients. They reported that heart rate decreases significantly ($p<0.01$) from 10 min up to 15 min in xylazine group. Respiration decreased significantly at 10 min and values remained significantly ($p<0.01$) lower than the base value. There was a slight and non-significant ($p>0.05$) decrease in RT at 10 min, which decreased significantly ($p<0.05$) at 15 min and it remained significantly ($p<0.01$) less from 30 min until the end of observation period in xylazine group. There was non-significant ($p>0.05$) increase in SBP from 10 to 15 min time interval in xylazine group. SpO_2 remained almost similar or slightly increased non-significantly at different time intervals.

Yadav *et al.* (2016) compared the stability and efficacy of acepromazine, dexmedetomidine and xylazine as preanaesthetics in propofol-halothane anaesthesia in dogs. In which glycopyrrolate and butorphanol were administered in all the animal @ 0.01 mg/kg and 0.2 mg/kg, respectively. All the preanaesthetic combination produces mild to moderate sedation. They reported that clinic-physiological parameters in animals of all groups altered within physiological limit and then nearly normalized at complete recovery.

Arunkumar *et al.* (2017) evaluated clinical and physiological effects of dexmedetomidine, xylazine and triflupromazine as preanaesthetics with propofol-isoflurane anaesthesia for various surgeries in dogs. The rectal temperature decreased nonsignificantly in xylazine treated dogs. Respiratory rate decreased significantly ($P\leq0.01$) throughout the study period in xylazine-propofol anaesthesia. Analgesia was good, with complete loss of pedal reflex, in three groups. However, analgesia was better in xylazine group dogs than in dexmedetomidine group and triflupromazine group dogs.

Chandrakala *et al.* (2017) studied clinical and haemato-biochemical alterations following administration of tramadol as preanaesthetic analgesic with xylazine and propofol anaesthesia in canine ovariohysterectomy. They observed non-significant ($P>0.05$) decrease in the rectal temperature at 10, 20and 30 min intervals and

thereafter it decreased further and turned out to be significant (P<0.05) in comparison to the base line whereas; respiration rate showed a significant (P<0.05) decrease at 30 min as compared to baseline and heart rate reduced gradually from the base line up to 60 min.

Sahoo *et al.* (2018) compared sedative effect of dexmedetomidine/ xylazine in combination with butorphanol-midazolam as preanaesthetic to ketamine anaesthesia for ovariohysterectomy in dogs. They reported adequate muscle relaxation, sedation and analgesia were excellent along with smooth and uneventful recovery after xylazine administration. Onset of sedation and induction time was quicker in dexmedetomidine group. Pedal reflex, palpebral reflex, jaw tone and muscle relaxation were mild after dexmedetomidine and xylazine administration. Rectal temperature, heart rate and respiration rate decrease non-significantly from base value after xylazine administration.

Aslam *et al.* (2019) studied clinico-biochemical effects of different pre anesthetic drugs combined with propofol for neutering dogs. In which xylazine 2.2 mg/kg, diazepam 0.25 mg/kg and medetomidine 40 µg/kg body weight, were injected intramuscular as preanaesthetics in A, B and C groups. After 3-5 minutes of preanesthetic, the propofol injection @ 6 mg/kg of body weight was administered intravenous as anesthetic drug in all three groups. A non-significant reduction was observed in rectal temperature of all treatment groups. Pulse rate initially decrease in medetomidine and xylazine treated groups due to peripheral vasoconstriction followed by vasodilatation. Respiratory rate depression was observed in all three groups due to direct depression of respiratory centre in central nervous system.

Bhave *et al.* (2019) studied clinical efficacy of propofol and Ketofol anaesthesia with butorphanol by constant rate infusion using fluid bag technique in dogs. In which all the patients were sedated with xylazine at 2 mg/kg b.wt. Group A was induced with propofol @4 mg/kg and Group B with Ketofol (1:1) @ 4 mg/kg by intravenous bolus administration. Maintenance was carried out by constant infusion of anaesthetic drugs at 6 mg/kg/hr at 5 ml/kg/hr flow rate in both the groups. They reported that heart rate, rectal temperature and respiratory rate decrease non-significantly between the groups but the values were within normal limits.

2.3.2 Hemato-Biochamical Effects

Fani *et al.* (2008) studied haematological and biochemical changes during epidural xylazine hydrochloride anaesthesia in dogs. They reported that

haematological parameters *viz*. TEC, PCV, Hb decreases significantly and TLC decreases non-significantly. They found significant increase in serum glucose value while SGPT and BUN significantly altered whereas no change in serum creatinine.

Dugdale (2010) reported that haematological effects like cell counts and total protein may decrease slightly with the use of alpha 2 adrenergic agonists. Increase in blood glucose after alpha-2 adrenergic agonist is common. Packed cell volume is decrease due to splenic sequestration. Total protein value decreases due to a shift of fluid into the intravascular space secondary to hyperglycaemia.

Sharma and Bhardwaj (2010) comparatively evaluated propofol alone and along with xylazine or midazolam in healthy dogs. They reported that Haemato-biochemical parameters showed non-significant changes in their values during the entire observation period.

Çamkerten *et al.* (2013) studied haematological and biochemical effects of xylazine-ketamine anesthesia on greyhounds. The animals were injected with the ketamine (10 mg/kg) and xylazine (1 mg/kg) intramuscularly. Haematological and biochemical findings were recorded before and during anesthesia. They reported no significant differences between baseline and during anesthesia values of hematological (WBC, RBC, PLT, HCT and Hb) and biochemical (AST, ALT and Creatinine) parameters. They also reported that blood Glucose increases and total protein were significantly decrease significant than before anesthesia.

Jena *et al*. (2014) evaluated and compared the clinico-physiological, hemodynamic and hematobiochemical effects in response to different total intravenous anaesthesia techniques using xylazine or dexmedetomidine with propofol in canine patients. They reported that Hb and PCV showed a non-significant increase at 30 min in xylazine group. Blood glucose showed a non-significant increase in xylazine group. Blood urea nitrogen and creatinine showed non-significant decrease at 30 min followed by a non-significant increase at 60 min in both the groups. TLC showed a non-significant decrease at 30 min, followed by a significant ($p<0.05$) decrease at 60 min in xylazine-propofol group. Neutrophil count showed non-significant increase in both the groups whereas lymphocyte count showed a significant decrease in xylazine group. Eosinophil count showed a non-significant increase in xylazine group.

Khan *et al.* (2014) studied haemoglycemic effects of xylazine, diazepam and ketamine in surgically treated dogs. They reported xylazine induced smooth sedation

with good analgesia and muscle relaxation. Blood glucose was significant increase after xylazine sedation till 2 hours followed by no significant difference till 8 hours.

Dewangan *et al.* (2016) studied haemato-biochemical response to xylazine-propofol anaesthesia in dogs. In which Xylazine @ 1mg/kg was administered intramuscularly 10 min. prior to the injection of propofol @ 4mg/kg in all the dogs. They reported that non-significant decrease in haemoglobin, packed cell volume and total erythrocyte count while non-significant increase in total leucocyte count was observed. The biochemical parameters viz., glucose, BUN, creatinine, AST and ALT showed significant ($P<0.01$) increase up to 35 minutes post anaesthesia however these values returned to near normal by 60 minutes. Total proteins decreased non-significant at 20 min.

Chandrakala *et al.* (2017) evaluate the haemato-biochemical profiles following administration of ketamine or butorphanol as preanaesthetic analgesic in xylazine - propofol anaesthesia in elective ovariohysterectomy procedure. They reported lymphocytopenia and relative neutrophilia was common; where as other haematological parameters did not reveal any significant changes. The BUN, creatinine, ALT and AST were non-significantly variables, whereas, increase glucose was the noticed at 1 hr interval in both the groups. Changes in total protein were transiently variable. In conclusion, transient variables were within the physiological limits have been reported following ketamine or butorphanol as preanaesthetic analgesic in xylazine and propofol induced anaesthesia which further maintained with continuous rate infusion of propofol @0.3 mg/kg/min. Hence, these combinations of anaesthesia can be used safely in compromised animal and clinically healthy animals.

Chandrakala *et al.* (2017) studied clinical and haemato-biochemical alterations following administration of tramadol as preanaesthetic analgesic with xylazine and propofol anaesthesia in canine ovariohysterectomy. They reported haemoglobin, packed cell volume, total leucocytic counts and differential leucocytic counts except lymphocytes exhibited non- significant fall ($P>0.05$) at different intervals. A variable and consistent increase ($P>0.05$) in glucose, blood urea nitrogen, creatinine, ALT and total protein could be noticed at different intervals after administration of drugs.

Aslam *et al.* (2019) studied clinico-biochemical effects of different pre anesthetic drugs combined with propofol for neutering dogs. In which xylazine 2.2 mg/kg, diazepam 0.25 mg/kg and medetomidine 40 µg/kg body weight, were injected intramuscular as preanaesthetics in A, B and C groups. After 3-5 minutes of

preanesthetic, the propofol injection @ 6 mg/kg of body weight was administered intravenous as anesthetic drug in all three groups. They reported that CBC, ALT, AST, ALP and blood urea nitrogen values were non-significantly in all the groups. There was non-significant decrease in Hb and total erythrocytes count while non-significant increase in total leukocyte count was noted in all three groups.

2.4 PROPOFOL

Propofol is a rapid acting, nonbarbiturate and relatively noncumulative IV anaesthetic (Branson and gross, 1994 and Muir and Hubbell, 2000). It produces satisfactory sedation with good hemodynamic stability and fast, unexcited recovery (Weaver and Raptopoulos, 1990). Propofol is a non-barbiturate alkyl phenol derivative hypnotic used alone and along with other preanaesthetics (Bufalari *et al.*, 1998).

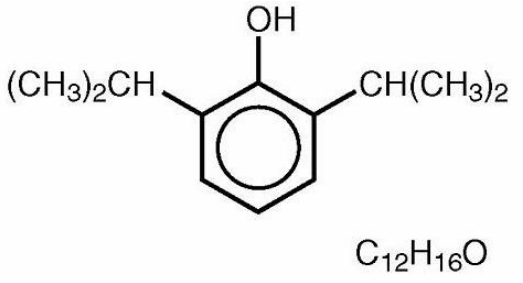

Fig. 2.4 Chemical structure of propofol

Propofol is a non-barbiturate short acting intravenous agent which has the potential of being used for induction of anesthesia (Glowaski and Wetmore, 1999). The advantages of propofol includes; rapid action, excellent hypnosis, good muscle relaxation, a non-cumulative effect and rapid complete recovery (Adetunji *et al.*, 2002). Induction of anaesthesia with propofol is accompanied by a decrease in arterial pressure in association with decreases in cardiac output and systemic vascular resistance (Prys-Roberts *et al.*, 1983; Aun and Major, 1984 and Stephen *et al.*, 1986).

Propofol is an intravenous anesthetic agent chemically unrelated to barbiturates or other anesthetic agents. Propofol is a member of the alkyl phenol family. It is available as white, ready-to-use, oil-inwater emulsion containing 10% soya bean oil, 2.25% glycerol, 1.2% purified egg phosphatide and 1% propofol sealed in 20 ml vials. It has a neutral pH, is isotonic and because of its formulation it is effective only when administered by intravenous injection. Propofol anesthesia in dogs is characterized by rapid onset; short duration; rapid metabolism; lack of

cumulation on repeated administration; some respiratory depression and rapid, smooth recovery from anesthesia.

2.4.1 Clinico-Physiological Effects

Goodchild and Serrao (1989) studied cardiovascular effects of propofol in the anaesthetized dog. They conclude that anaesthesia with propofol may be accompanied by decreased cardiac output secondary to reduction in preload by a direct vasodilator effect. They suggest that cardiac output and arterial pressure are preserved well at normal anaesthetic blood concentrations of propofol if the preload is maintained.

Bufalari *et al.* (1998) studied the use of propofol as an induction agent for halothane and isoflurane anesthesia in dogs. They observed that no induction apnea occurs after propofol. They reported that the initial propofol mediated decrease in arterial blood pressure continued during either halothane (52.4%) or isoflurane (38%) anesthesia without a simultaneous increase in heart rate. No significant metabolic and hematological abnormalities were recorded in all the dogs. In both groups, induction of anesthesia was not only rapid but also smooth and without excitatory effects. A temporary increase in pulse rates occurred in both groups after propofol induction. Mean arterial blood pressure decreased after the first 10 minutes of anesthesia in both the groups and then stabilized. Mean SpO_2 remained greater than 90% in both groups at two and five minutes after induction. They concluded that Propofol (6.6 mg/kg body weight, IV) produced safe, smooth, reliable anesthetic induction without adverse effects over 60 seconds in non-premedicated dogs. Propofol, in combination with inhalant agents, can be used effectively and safely for canine anesthesia in veterinary practice.

Short and Bufalari (1999) suggested that Propofol can induce significant depression of respiratory function, characterized by a reduction in the rate of respiration. Potent alpha-2 sedative/ analgesics (e.g., xylazine, medetomidine) or opioids (e.g., oxymorphone, butorphanol) increase the probability of respiratory depression during anesthesia. Appropriate consideration of dose reduction and speed of administration of propofol reduces the degree of depression. Cardiovascular changes induced by propofol administration consist of a slight decrease in arterial blood pressures (systolic, mean, diastolic) without a compensatory increase in heart rate.

Kuusela *et al*. (2001) compared medetomidine and dexmedetomidine as premedicant in dogs undergoing propofol-isoflurane anesthesia and reported

significant increase in heart rate after induction with propofol whereas; mean arterial pressure decreased gradually and significantly after induction. Respiration rate decreased significantly after induction in M4/D2 and M40/D20 premedicated dogs. No significant difference was observed in SpO_2 and it varied between 97 and 100%. They reported high total sedation score (Posture scores, palpebral reflex, eye position, jaw and tongue relaxation, resistance to positioning in lateral recumbency and general appearance) which indicate deep sedation in dexmedetomidine premedication.

Kuusela *et al.* (2003) compared propofol infusion and propofol/isoflurane anaesthesia in dexmedetomidine premedicated dogs. They reported that heart rate in propofol group was significantly lower than in the isoflurane group and significantly higher when compared with controls during anaesthesia to extubation. MAP in the propofol group was significantly higher than in isoflurane group and similar to controls during anaesthesia. Respiration rate did not differ between treatments during anaesthesia. They reported palpebral reflexes were completely abolished, ventrally deviated eye ball during isoflurane anaesthesia. Induction and recovery were always smooth without any signs of nausea.

Mukati *et al.* (2006) studied clinico-physiological effects of propofol alone and in combination with xylazine or acepromazine in dogs. They reported significant increase in pulse and heart rate and non-significant decrease in body temperature after induction. The respiration rate increased significantly in propofol alone.

Seliskar *et al.* (2007) evaluated the cardiorespiratory parameters, the depth of anaesthesia and the quality of recovery in dogs that had been premedicated with medetomidine @ 40 μg/kg administered with either propofol @ 1 mg/kg followed by 0·15 mg/kg/minute, intravenously or with ketamine @ 1 mg/kg followed by 2 mg/kg/hour, intravenously and propofol @ 0·5 mg/kg followed by 0·075 mg/kg/minute, intravenously. The dogs heart rate and mean arterial blood pressure were higher and their minute volume of respiration and temperature were lower when they were anaesthetized with propofol plus ketamine. When the dogs were anaesthetized with propofol alone they recovered more slowly but uneventfully.

Enouri *et al.* (2008) evaluate the cardiopulmonary effects of anesthetic induction with thiopental, propofol or ketamine hydrochloride and diazepam in dogs sedated with medetomidine and hydromorphone. They reported significant decrease in heart rate and respiration rate in propofol group. Mean arterial blood pressure was

significantly higher than baseline values in propofol group. Body temperature decreased during the experimental period for all induction regimens.

Lin *et al.* (2008) evaluated cardiovascular and respiratory effects and pharmacokinetics of a 24hour intravenous constant rate infusion (CRI) of dexmedetomidine during and after propofol or isoflurane anaesthesia in dogs. They reported decrease in heart rate induced by dexmedetomidine were greater for propofol than isoflurane. Oxygen saturation was maintained in normal range. DAP and SAP were higher than baseline at all time points for propofol, but not for isoflurane.

Moezzi *et al.* (2014) evaluated electrocardiographic parameters in healthy dogs anesthetized with ketamine-propofol combination (ketofol) and medetomidine, acepromazine and acepromazine-morphine as preanesthetic agents. They reported that heart rate decreases significantly in medetomidine groups.

Bolaji-Alabi *et al.* (2018) evaluated effects of oxygen supplementation on propofol anesthesia in acepromazine/tramadol premedicated dogs. Six Nigerian indigenous dogs were premedicated with intramuscular injection of acepromazine @ 0.03 mg/kg and tramadol @ 5 mg/kg, followed by induction of anesthesia with propofol @ 4 mg/kg IV 20 min later. Anaesthesia was maintained by repeated bolus injections of propofol @ 2 mg/kg at 10 min interval for 2 hours and anesthetized dogs breathed oxygen. Mean heart rate and rectal temperature was progressively decreased from the 60 min interval in all the dogs however; no change in $SpO_2$was seen in both experimental trials.

Thejasree *et al.* (2018) evaluated propofol and ketofol anaesthesia following atropine, diazepam and fentanyl premedication in dogs. All the animals were randomly divided into two groups in which Ketofol (1:1) combination was given intravenously in group I and Propofol @ 6 mg/kg BW intravenously were given in group II dogs. Induction quality was excellent, smooth and attained sternal recumbency rapidly without struggling in all animals of both the groups. Recovery from anaesthesia was smooth and excitement free in both groups. Decrease in rectal temperature was recorded in both groups during anaesthesia and surgery. Hypothermia was probably produced by the sedatives and anaesthetics used, which decreased rectal temperature by depression of thermoregulatory centre, reduced basal metabolic rate and muscle activity, depression of peripheral circulation and vasodilatation (Weaver and Raptopoulus 1990 and Thurmon *et al.,* 1995). A

significant decrease in respiratory rate and pulse rate was observed in dogs subjected to propofol anaesthesia following premedication and induction of anaesthesia.

Dinesh *et al.* (2019) evaluated efficacy and safety of atropine- midazolam pentazocine with propofol/ketamine for induction and isoflurane for maintenance of anaesthesia in dogs undergoing orthopaedic surgical procedures. They reported that the mean values of respiratory rate and heart rate were statistically higher in ketamine group than propofol group at different time interval during anaesthesia. However, the values of rectal temperature at different interval in all the dogs were statistically similar. Induction score of propofol group is higher. Time for drooping of eyelids, loss of palpebral reflex, rotation of eye ball, relaxation of jaw muscles, loss of tongue reflex, loss of swallowing reflex and intubation are lower in propofol group compared to ketamine group. They stated that propofol was found to produce more smooth and rapid induction.

2.4.2 Haemato-Biochemical Effects

Enouri *et al.* (2008) evaluated the cardiopulmonary effects of anaesthetic induction with thiopental, propofol or ketamine hydrochloride and diazepam in dogs sedated with medetomidine and hydromorphone. They founded that PCV was higher after administration of the preanaesthetic medications and after administration of the induction doses, compared with the value at baseline, whereas PCV was lower during isoflurane administration than after administration of preanaesthetic medications or after administration of induction doses. Mean total protein concentration for all induction regimens was lower after administration of the preanesthetic medications and continuing throughout the remainder of the experimental period, compared with the value at baseline.

Lin *et al.* (2008) evaluated cardiovascular and respiratory effects and pharmacokinetics of a 24-hour intravenous constant rate infusion of dexmedetomidine during and after propofol or isoflurane anaesthesia in dogs. They reported that haemoglobin and glucose increase in propofol as well as in isoflurane.

Thejasree *et al.* (2018) evaluated Propofol and Ketofol Anaesthesia Following Atropine, Diazepam and Fentanyl Premedication in Dogs. They reported that haemoglobin and packed cell volume decreased significantly in propofol anaesthesia. A non-significant increase in ALT was noticed in propofol anaesthesia.

Dinesh *et al.* (2019) evaluated efficacy and safety of atropine- midazolam pentazocine with propofol/ ketamine for induction and isoflurane for maintenance of

anaesthesia in dogs undergoing orthopaedic surgical procedures. They reported that haemoglobin and PCV values decrease non-significantly in propofol group. Decrease in these values might be due to the spleenic dilation resulting in splenic sequestration of R.B.C.s (Hewson *et al*., 2006 and Welberg *et al.*, 2006), shifting of fluid from extravascular compartment to intravascular compartment to maintain normal cardiac output (Wagner and Muir, 1991) during anaesthesia and due to loss of blood during surgery (Coles, 1986). Blood glucose increases non-significantly in propofol group. Plasma BUN and plasma creatinine increases non-significantly after administration of propofol. Due to anaesthesia and stress associated with surgery release of aldosterone, vasopressin, renin and catecholamines occurred (Lumb and Jones, 2007c). Plasma ALT decreases non-significantly after induction with propofol. Plasma total protein decrease non-significantly in propofol group.

2.5 ISOFLURANE

Isoflurane is a newer inhalant anesthetic with desirable pharmacologic and clinical properties. Its use is well established in veterinary medicine. Isoflurane has many positive characteristics such as low biodegradability, fast onset of action, and rapid recovery because of its relatively low blood solubility. As with all inhalant anesthetics, isoflurane depresses cardiovascular, pulmonary, and neuronal functions in a dose-dependent manner (Steffey and Howland, 1978). Compared to halothane, isoflurane is significantly less arrhythmogenic in dogs and cats (Hubbell *et al.*, 1984).

Klide (1976) studied cardiopulmonary effects of enflurane and isoflurane in the dog. He observed that isoflurane has better cardiopulmonary stability than enflurane however; the depression of cardiopulmonary function from both agents increased with increasing depth of anesthesia. He reported that isoflurane did not produce muscle twitching, but enflurane did.

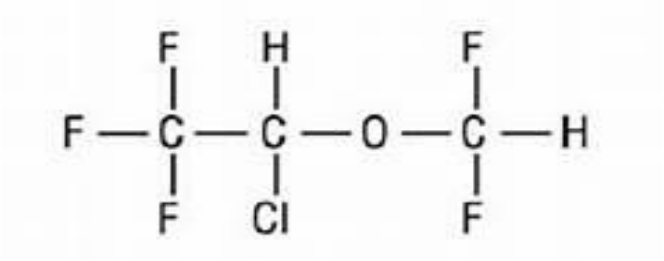

Fig 2.5 Chemical structure of isoflurane

Steffey and Howland, (1977) investigated cardiopulmonary effects of isoflurane in healthy unpremedicated dogs and cats. They found that as anesthetic dose increased, mean arterial pressure consistently and significantly decreased. Heart

rate significantly increased but stroke volume, total peripheral resistance and left ventricular work tended to decrease as anesthesia deepened. They found no significant difference in cardiovascular measurements.

Galloway *et al*. (2004) suggest that isoflurane is a more potent respiratory depressant than other volatile anaesthetics which must have contributed to decreased respiration rate.

Tsai *et al.* (2007) compared recovery from total intravenous anesthesia with propofol and inhalation anesthesia with isoflurane in dogs. They reported that dogs anesthetized with propofol-TIVA showed slower recovery than dogs anesthetized with isoflurane anesthesia.

2.5.1 Anaesthetic induction and recovery

Morgan and Legge (1989) evaluation of propofol as an intravenous anaesthetic agent in cats and dogs. They reported the mean induction doses of propofol for unpremedicated dogs and cats were 6.55 and 8.03 mg/kg b. wt., respectively while the mean induction doses of propofol for premedicated (acepromazine, diazepam and xylazine) dogs and cats which were 4.5 and 5.97 mg/kg b. wt., respectively. The mean recovery time was from 23 to 40 minutes in dogs and 27 to 38 minutes in cats.

Weaver and Raptopoulos (1990) studied induction of anaesthesia in dogs and cats with propofol. They reported the mean induction doses of propofol in unpremedicated and premedicated with acepromazine, papaveretum, diazepam, pethidine, atropine and scopolamine in different combinations were 5.2 ± 2.3 and 3.6 ± 1.4 mg/kg b. wt., respectively for dogs and 5.0 ± 2.8 and 5.3 ± 4.3 mg/kg b. wt., respectively for cats.

Hall *et al.* (1997) studied disposition of propofol after medetomidine premedication in beagle dogs. They suggested that the induction dose of propofol was 7.00mg/kg in non-premedicated compared with 3.09mg/kg in premedicated dogs.

Redondo *et al.* (1999) compared xylazine, medetomidine and romifidine as premedicant to propofol and halothane-N2O anaesthesia. In which all the animals were administered atropine @ 10µg/kg IM. Xylazine and medetomidine were administered @ 1 mg/kg and 20µg/kg in xylazine group and medetomidine group respectively. Anesthesia was induced with intravenous administration of propofol at a slow dose-effect rate with small boluses until a plane of anesthesia suitable for endotracheal intubation was achieved. They stated that propofol produce satisfactory quality of induction of anaesthesia without excitation in all the animals. There was no

any difficulty in endotracheal intubation. Induction dose of propofol were 1.80 ± 0.46 mg/kg and 2.56 + 0.96 mg/kg for medetomidine and xylazine, respectively. They reported that marked synergism between α2-agonists and propofol.

Lerche *et al.* (2000) compared the effects of propofol alone or propofol and ketamine for the induction of anaesthesia in dogs. Anaesthesia was induced with propofol (4 mg/kg bodyweight intravenously) or propofol and ketamine (2 mg/kg bodyweight of each intravenously). They reported that induction aponea was more common in propofol followed by ketamine than propofol alone. Recovery time remain similar in both the groups**.** Heart rate, respiratory rate and systolic blood pressure was significantly decrease after the induction of anaesthesia ($P<0.001$) in both the groups. Decrease in heart rate was greater after induction with propofol.

Kuusela *et al*. (2001) reported that propofol required for induction was affected by dose level of premedication. Dexmedetomidine produces dose dependent sedation and analgesia in dogs means sedation and analgesia increase with increase in dose. Doses of propofol required for induction were 5.8 ± 1.0 mg/kg; 6.0 ± 1.1 mg/kg, 2.7 ± 0.3 mg/kg, 2.7 ± 0.5 mg/kg, 0.9 ± 0.3 mg/kg; and 0.8 ± 0.2 mg/kg for M0.4, D0.2, M4, D2, M40 and D20 respectively.

Kuusela *et al*. (2003) compared propofol infusion and propofol/isoflurane anaesthesia in dexmedetomidine premedicated dogs. They concluded that propofol infusion produced more respiratory depression than propofol/isoflurane in dogs premedicated with dexmedetomidine. Recovery was delayed after propofol treatment. They concluded that propofol/isoflurane anaesthesia was considered more useful than propofol infusion because of milder degree of respiratory depression and faster recovery. Dexmedetomidine-propofol combination lengthened the recovery.

Gomez-villamandos *et al.* (2006) evaluate dexmedetomidine as a premedicant in dogs prior to propofol-desflurane anaesthesia. They reported intravenous dexmedetomidine produced satisfactory sedation allowing easy handling of the dogs. The quality of induction of anaesthesia with propofol was satisfactory and without excitement in all the cases and there were no difficulties in endotracheal intubation. The mean (±SD) dose requirement of propofol for induction was 3.1 ± 0.4 mg/kg, 2.8 ± 0.3 mg/kg in dexmedetomidine @ 1 µg/kg and 2 µg/kg respectively. Intravenous administration of propofol produced excitement free induction of anaesthesia in all dogs.

Mukati *et al.* (2006) studied clinico-physiological effects of propofol alone and in combination with xylazine or acepromazine in dogs. The time of induction of anaesthesia was 43.50 ± 1.78, 33.83 ± 1.96 and 37.00 ± 2.18 sec; duration of anaesthesia was 8.70 ± 0.60, 21.66 ± 1.05 and 11.06 ± 0.42 min whereas mean time of complete recovery was 15.16 ± 0.47, 33.50 ± 1.58 and 21.66 ± 0.91 min in propofol, xylazine-propofol and acepromazine-propofol, respectively. They reported smooth and excitement free recovery in all the treatments.

Enouri *et al.* (2008) evaluated the cardiopulmonary effects of anesthetic induction with thiopental, propofol or ketamine hydrochloride and diazepam in dogs sedated with medetomidine and hydromorphone. Dose of the induction agent that enabled endotracheal intubation was 1 mg/kg of propofol after preanaesthetic administration. Induction of anesthesia was smooth and intubation was easily performed in all dogs at these doses.

Alkattan and Helal (2013) suggested that the anesthetic protocol of propofol as induction agent and halothane as maintenance anesthesia induced a good quality anesthesia with a short duration of action and rapid smooth recovery without complications in dogs.

Raszplewicz *et al*. (2013) compared sedation scores and propofol induction doses in dogs receiving either dexmedetomidine (5 μg/kg) or medetomidine (10 μg/kg), both with butorphanol intramuscularly (IM) prior to general anaesthesia. There was no statistically significant difference in propofol anaesthetic induction dose evaluated 45 minutes after premedication between the two groups. They reported that butorphanol-medetomidine produced effective sedation than butorphanol-dexmedetomidine in dogs but this did not significantly affect the induction dose of propofol required for anaesthesia.

Jena *et al.* (2014) carried out clinical evaluation of total intravenous anaesthesia using xylazine or dexmedetomidine with propofol in dogs. They found that dogs showed quicker attenuation of reflexes in dexmedetomidine group. Induction doses of propofol were 3.17±0.21 and 2.72±0.15 mg/kg BW and rate of infusion of propofol for maintenance of anaesthesia were 0.33±0.02 mg/kg/min and 0.35±0.02 mg/kg/min, respectively in animals premedicated with xylazine and dexmedetomidine. Recovery was quicker in dexmedetomidine group. Physiological, haemodynamic and haemato-biochemical parameters were non-significantly variables in both the groups.

Ferreira *et al.* (2015) studied anaesthetic induction and recovery characteristics of diazepam-ketamine combination with propofol alone in dogs undergoing elective orchidectomy. They reported that propofol had better quality of recovery and shorter recovery times compared with diazepam-ketamine group.

Diao *et al.* (2016) reported that induction dose of propofol was 6.0±1.4 mg/kg and 3.7±0.4 mg/kg in propofol alone and dexmedetomidine- propofol combination respectively. They reported shorter recovery time with propofol-isoflurane combination as compared to CRI propofol with dexmedetomidine.

Arunkumar *et al.* (2017) evaluated Clinical and physiological effects of dexmedetomidine, xylazine and triflupromazine as preanaesthetics with propofol-isoflurane anaesthesia for various surgeries in dogs. They reported time for onset of sedation, induction time, duration of anaesthesia and recovery time were 2.05±0.19 minutes, 57.33±0.99 seconds, 94.17±11.50 minutes and 22.33±3.12 minutes, respectively after dexmedetomidine-propofol-isoflurane anaesthesia. Whereas, time for onset of sedation, induction time, duration of anaesthesia and recovery time were 3.33±0.48 minutes, 58.50±1.54 seconds, 67.17±12.50 minutes and 18.17±1.83 minutes respectively after xylazine-propofol-isoflurane anaesthesia. They suggested that the induction and recovery were smooth and uneventful in all groups.

Mate and Aher (2019) observed that the dose of propofol was reduced to 1.22 ± 0.23 mg/kg body weight after butorphanol-dexmedetomidine preanaesthetic in dogs.

CHAPTER – III

MATERIALS AND METHODS

The present clinical study entitled "Evaluation of anaesthetic regimen using butorphanol and xylazine/dexmedetomidine as preanaesthetics, propofol as induction agent and isoflurane as maintenance anaesthetic in dogs" was conducted in twelve dogs at the Department of Veterinary Surgery and Radiology in collaboration with Veterinary Clinical Complex and Department of Veterinary Pathology, College of Veterinary Science and Animal Husbandry, Kamdhenu University, Navsari.

3.1 SELECTION OF ANIMALS

The study was conducted in 12 dogs presented for surgical intervention at Department of Veterinary Surgery and Radiology, College of Veterinary Science and Animal Husbandry, Navsari. All these animals were randomly divided into two groups (n=6) irrespective of age, breed, sex, body weight and surgical complaint.

3.2 PREANAESTHETIC EVALUATION AND PREPARATION

Preanaesthetic evaluation of the patient was carried out by obtaining history regarding breed, age, sex, chief complaint and duration of illness. All the dogs were fasted for 12 hours and water was withdrawn for 6 hours prior to surgery. Weighing of each dog was done for calculating the exact dose of the anaesthetic drugs.

3.3 ANAESTHETIC PROTOCOL

The selected animals were randomly divided into two groups (n=6 each). All the animals were first premedicated with butorphanol[1] @ 0.2 mg/kg BW, intramuscularly and then after 15 minutes, dexmedetomidine[2] @ 5µg/kg BW and xylazine[3] @ 0.5 mg/kg BW was administered intravenously in group I and II, respectively.

The anaesthesia was induced by intravenous administration of 1% propofol[4] till effect in both the groups five minutes after administration of preanaesthetic and the animals were intubated.

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[1] **Butorphanol:** Inj. Butrum-2, Butorphanol tartrate 2 mg/ml, Aristo pharmaceuticals Pvt. Ltd., M.P.
[2] **Dexmedetomidine:** Inj. Dexmeto 100 mcg/ml, Miracalus Pharma Pvt. Ltd., Mumbai.
[3] **Xylazine:** Inj. Xylaxin, Xylazine HCL 23.32 mg/ml, Indian Immunological Ltd., Telangana, India.
[4] **Propofol**: Inj. Dipventin, Propofol injection 10 mg/ml, Naprod Life Sciences Pvt. Ltd, Thane.

Anaesthesia was maintained by isoflurane[5] with 100% oxygen in all the animals through small animal inhalation anaesthesia machine[6]. The vaporizer[7] setting was adjusted according to the depth of anaesthesia after monitoring the animal's response. Details of anaesthetic protocols of different groups are given in table 3.1.

Table 3.1: Anaesthetic Protocols

Group	Preanaesthetic agents	Induction agent	Maintenance agent
I (n=6)	Butorphanol @ 0.2 mg/kg IM + Dexmedetomidine @ 5µg/kg IV	1 % Propofol (Till effect, IV)	Isoflurane
II (n=6)	Butorphanol @ 0.2 mg/kg IM + Xylazine @0.5 mg/kg IV		

3.4 EVALUATION OF ANAESTHETIC PROTOCOLS

Anaesthetic protocols were evaluated on the basis of the following findings.

3.4.1 Anaesthetic Parameters

3.4.1.1 Dose of induction agent

The dose of 1% propofol in both the groups was calculated in milligrams per kilogram body weight of the animals.

3.4.1.2 Duration of maintenance anaesthesia

Time elapsed in minutes from starting of isoflurane administration to cessation of isoflurane administration was calculated as duration of maintenance anaesthesia.

3.4.1.3 Duration of surgery

Time elapsed in minutes from starting of skin incision till the last skin suture taken was calculated as time taken for surgery.

3.4.1.4 Total duration of anaesthesia

Time elapsed in minutes from disappearance to reappearance of pedal reflex was calculated as duration of anaesthesia.

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[5] **Isoflurane**: Isoflurane USP 250 ml, Raman & Weil Pvt. Ltd., Daman, India.

[6] **Small animal inhalant anaesthetic machine:** Landmark USA-2100, Vetland Medical Sales & Services, Kentucky, USA.

[7] **Vaporizer**: Drager D 19.1 Vaporizer, Vetland Medical Sales & Services, Kentucky, USA.

3.4.1.5 Recovery time

Time elapsed in minutes from cessation of isoflurane administration to reappearance of pedal reflex was calculated as recovery time.

3.4.1.6 Quality of sedation (Singh *et al.*, 2012)

Quality of sedation was assessed before induction of anaesthesia by a scoring system graded on 1 to 4 score scale.

1	Animal appears alert.
2	Decreased alertness, some response to touch.
3	Animal calm, minimal restraint needed, eyelid partially closed and sluggish palpebral reflex.
4	Animal totally calm, no restraint needed, eye lids closed and very weak palpebral reflex.

3.4.1.7 Quality of induction (Singh *et al.*, 2012)

Quality of induction was assessed after intubation by scoring system graded on 1 to 4 score scale.

1	Marked excitement, struggling, vocalization, urination or defecation. Firm restraint required.
2	Moderate excitation gross movement, vocalization, urination or defecation. Firm restraint required.
3	Transition associated with some movements requiring restraint by a single assistant.
4	Smooth and rapid transition from conscious to anaesthetized state.

3.4.1.8 Quality of maintenance anaesthesia

Quality of maintenance anaesthesia was evaluated on the basis of resistance of jaw, palpebral reflex, pedal reflex graded on 0 to 4 scale bases and eyeball position graded on 1 to 4 scale bases (Singh *et al.,* 2012). All the reflexes were evaluated before administration of preanaesthetics, after induction and thereafter at every 10 minutes up to 50 minutes.

3.4.1.8.1 Pedal reflex

Pedal reflex; the index to judge the depth of anaesthesia was measured by observing the response of withdrawal of limb on pinching the interdigital skin with allies tissue forceps and graded as below

0	Intact and strong withdrawal
1	Intact but weak withdrawal
2	Very weak withdrawal
3	Very sluggish withdrawal
4	Abolished reflex

3.4.1.8.2 Palpebral reflex

Palpebral reflex was noticed for measuring the depth of maintenance anaesthesia by touching the medial canthus with index finger and observing the blink of eye lids. It was graded as below

0	Intact and strong reflex (Quick blink)
1	Intact but weak reflex (Slow response)
2	Very weak reflex (Very slow and moderate response)
3	Very sluggish reflex (Mild and occasional reflex)
4	Abolished reflex

3.4.1.8.3 Jaw tone

Jaw relaxation was taken as an index of muscle relaxation and measured by finding the resistance in opening of the jaw on applying traction over lower and upper jaws and graded as below

0	Not allowing to open the jaws (Tightly closed jaws)
1	Marked resistance to opening of jaws (Jaws close quickly)
2	Moderate resistance to opening the jaws (Jaws close quickly)
3	Mild resistance to opening of jaws (Jaws close slowly)
4	No resistance to opening of jaws (Jaws remain open)

3.4.1.8.4 Eyeball position

Position of eyeball was observed and graded as below

1	No rotation of eyeball
2	Slight rotation
3	Moderate rotation
4	Complete ventromedial rotation.

3.4.1.9 Quality of recovery (Singh *et al.*, 2012)

Recovery quality was evaluated on 1 to 4 score.

1	Excitement and paddling when recumbent, severe ataxia on standing
2	Some excitement and ataxia, paddling when attempts to stand, moderate ataxia on standing.
3	No excitement or struggling, mild ataxia on standing.
4	No ataxia, no staggering on standing.

3.4.2 CLINICO-PHYSIOLOGICAL PARAMETERS

The clinico-physiological parameters *viz*; rectal temperature (ºF), pulse rate (beats/minute), systolic blood pressure (mm Hg), diastolic blood pressure (mm Hg), mean arterial pressure (mm Hg) and peripheral saturation of oxygen (%) were recorded before administration of preanaesthetics, prior to induction, after induction of anaesthesia and thereafter at every 10 minutes interval up to 50 minutes using vital signs monitor[8].

Respiration rate (breaths/minute) was measured by counting the movement of thoraco-abdominal excursions before giving preanaesthetics and then by counting movement of rebreathing bag after induction of anaesthesia and thereafter every 10 minutes up to 50 minutes.

3.4.3 HAEMATO-BIOCHEMICAL PARAMETERS

The blood samples (2 ml) were collected from cephalic or recurrent tarsal vein (depending on IV cannula fixation) in K_3 EDTA test tubes before administration of preanaesthetics, prior to induction, after induction of anaesthesia and thereafter at every 15 minutes interval up to 45 minutes for

[8] **Vital signs monitor**: BM5 VET, Bionet Company Ltd, Seoul, South Korea.

haemato-biochemical studies. Further, at every time the blood smears were also prepared from the blood for differential leucocyte count.

3.4.3.1 Haematological Parameters

Haematological parameters *viz;* haemoglobin (g per cent), packed cell volume (per cent), total erythrocyte count (million/cu.mm) and total leucocytes count (thousand/cu.mm) were estimated using automatic haemato-analyzer[9] within 2 hours of blood collection while the blood smears were used for determination of differential leukocyte count (per cent) as described by Schalm *et al*. (1975).

3.4.3.2 Biochemical Parameters

The blood glucose (mg/dl) was estimated by using glucometer[10] immediately after the blood collection. After estimation of haematological parameters remaining volume of the blood was used for plasma separation by centrifugation at 3000 revolutions per minute for 10 minutes and stored at -20ºC in deep freezer for biochemical analysis. Biochemical parameters *viz;* total plasma protein (g/dl), alanine amino transferase (IU/L), blood urea nitrogen (mg/dl) and creatinine (mg/dl) were quantified by using semi-automatic biochemical analyzer[11] and standard kits.

3.5 COMPLICATIONS

Any complication or specific finding observed during the protocol was recorded.

3.6 STATISTICAL ANALYSIS

Data were analyzed using R software version 4.0.3 to estimate the mean. Means were compared using ANOVA and Duncan's New Multiple Range Test (DNMRT).

[9] **Automatic haemato-analyzer:** EXIGO CA 630 VET, Boule Medical AB, Sweden.
[10] **Glucometer**: Dr. Morpean Gluco One, Morpean Laboratories Limited, New Delhi, India
[11] **Semi-automatic biochemical analyzer**: Micro Lab 300, Vital Scientific, Netherlands.

CHAPTER-IV

RESULTS AND DISCUSSION

The present clinical study entitled “Evaluation of anaesthetic regimen using butorphanol and xylazine/dexmedetomidine as preanaesthetics, propofol as induction agent and isoflurane as maintenance anaesthetic in dogs” was carried out at the Department of Veterinary Surgery and Radiology, College of Veterinary Science and Animal Husbandry, Kamdhenu University, Navsari.

The obtained result are noted and discussed as under.

4.1 SELECTION OF ANIMALS

The study was conducted in 12 dogs (6 males and 6 females) of different breeds presented for surgical interventions at Department of Veterinary Surgery and Radiology. The age of the animals ranged from 0.37 years to 12 years with an average age of 5.86±1.21 years. The body weight of the animals ranged from 13 kg to 43 kg with average of 20.58±2.60 kg.

4.2 EVALUATION OF ANAESTHETIC PROTOCOLS

4.2.1 Dose of Induction Agent (Table 4.1)

In the present study, 1% propofol was used as induction agent in all the animals premedicated with butorphanol-dexmedetomidine and butorphanol-xylazine. The mean value of the induction dose rate of propofol was 0.90±0.13 in butorphanol-dexmedetomidine and 1.29±0.26 mg/kg in butorphanol-xylazine premedicated dogs.

Kuusela *et al.* (2001) reported that dose of propofol reduced to 2.7±0.5 mg/kg after administration of 2 µg/kg of dexmedetomidine. They found that degree of sedation and analgesia were significantly affected by dose levels but not by the drugs. Similarly, Gomez-villamandos *et al.* (2006) also reported reduction in propofol dose to 2.8±0.3 mg/kg after dexmedetomidine administration. Jena *et al.* (2014) reported that induction doses of propofol were reduced to 3.17±0.21 and 2.72±0.15 mg/kg BW with xylazine and dexmedetomidine premedicated dogs, respectively. Diao *et al.* (2016) reported that induction dose of propofol were 6.0±1.4 mg/kg and 3.7±0.4 mg/kg in propofol alone and dexmedetomidine-propofol combination, respectively. Mate and Aher (2019) reported that lowered dose of propofol (1.22±0.23 mg/kg) required for induction of anesthesia after butorphanol- dexmedetomidine in dogs.

Redondo *et al.* (1999) reported thatinduction dose of propofol is 1.80 ± 0.46 mg/kg and 2.56 + 0.96 mg/kg for medetomidine and xylazine, respectively. Morgan

and Legge (1989) reported that the induction dose of propofol was reduced from 6.55 mg/kg BW to 4.5 mg/kg BW after administration of xylazine, acepromazine and diazepam preanaesthetics in dogs.

The findings of above scientists collaborate with the results of the present study.

4.2.2 Duration of Maintenance Anaesthesia (Table 4.1)

In both the groups, isoflurane was used for maintenance of anaesthesia. The mean±SE value of maintenance anaesthesia was 65.83±6.32 and 71.83±12.49 minutes in group I and II, respectively. There was non-significant difference in the mean values of duration of maintenance anaesthesia between the groups in the present study. The variations in duration of maintenance anaesthesia between groups occurred due of different surgical procedures that were performed in both the groups.

4.2.3 Duration of Surgery (Table 4.1)

The mean±SE value of time taken for surgery was 59.33±5.81 in group I and 67.17±11.88 in group II. No significant difference was observed in the duration of surgery which varied depending upon type of surgical affections and the surgical procedures performed in the present study.

4.2.4 Total Duration of Anaesthesia (Table 4.1)

Propofol was used for induction of anaesthesia and maintained it was on isoflurane in both groups. The mean±SE value of total duration of anaesthesia was 73.17±5.78 minutes in group I and 80.33±13.03 minutes in group II. The non-significant difference in the mean values of anaesthesia was observed and the variation in the duration of anaesthesia was directly related to the surgical procedures included in the present study.

4.2.5 Recovery Time (Table 4.1)

The mean ± SE value of recovery time was 4.17±0.65 minutes in group I and 4.33±1.09 minutes in group II. Non-significant difference was observed in recovery time between the groups. Kuusela *et al.* (2003) and Diao *et al.* (2016) reported shorter recovery time with propofol-isoflurane combination as compared to CRI propofol with dexmedetomidine. Dexmedetomidine-propofol combination lengthened the recovery. Short recovery time observed might be caused by a lower blood gas partition coefficient of isoflurane. Similarly, Mukati *et al.* (2006) reported that mean time of complete recovery is 15.16±0.47 and 33.50±1.58 minutes in propofol alone and xylazine-propofol anaesthesia, respectively. Arunkumar *et al.* (2017) reported

recovery time of 22.33±3.12 and 18.17±1.83 minutes after dexmedetomidine-propofol-isoflurane and xylazine-propofol-isoflurane anaesthesia, respectively.

4.2.6 Quality of Sedation (Table 4.2)

Sedation score was observed excellent in all the animals of both the groups. The mean value of sedation quality was 4.00±0.00 in both the groups which showed no significant differences in sedation quality between the groups.

Greem *et al.* (2000) stated that butorphanol facilitated the fast sedation with α-2 agonists (dexmedetomidine and xylazine). Kuusela *et al.* (2001) stated that dexmedetomidine produces dose dependent sedation and analgesia in dogs. Gomez-villamandos *et al.* (2006) also reported that intravenous dexmedetomidine produced satisfactory sedation allowing easy handling of the dogs. Congdon *et al.* (2011) reported significant increase in sedation score from baseline after15 minutes of dexmedetomidine administration in dogs. Ahmad *et al.* (2013) reported that dexmedetomidine provided a reliably moderate sedation and analgesia in dogs.

Monterio *et al.* (2008) reported greater sedation with xylazine-methadone and acepromazine-methadone combination and they concluded that xylazine produce greater analgesia when used with opioids. Cassu *et al.* (2014) reported greater degree of sedation after intramuscular administration of xylazine at 15 minutes than phamacopuncture xylazine-Yintang. Khan *et al.* (2014) reported that xylazine induced smooth sedation with good analgesia and muscle relaxation. Yadav *et al.* (2016) reported that dexmedetomidine and xylazine produced mild to moderate degree of sedation with glycopyrrolate and butorphanol.

4.2.7 Quality of Induction (Table 4.2)

In the present study, propofol was used as induction agent in both the groups. The mean value of induction quality was 4.00±0.00 in both the groups. Successful endotracheal intubation was achieved in all the animals of both groups. Quality of induction was excellent with smooth and rapid transition from conscious to anaesthetized state with propofol. Kuusela *et al.* (2003); Gomez-villamandos *et al.* (2006); Enouri *et al.* (2008) and Diao *et al.* (2016) also reported that dexmedetomidine-propofol combination produced satisfactory quality of induction of anaesthesia without excitement. Similarly, Bufalari *et al.* (1998) and Thejasree *et al.* (2018) reported that propofol produced safe, smooth, reliable anesthetic induction without any adverse effects.

Redondo *et al.* (1999) reported that propofol produced satisfactory quality of induction anaesthesia without any complication in dogs with xylazine. Arunkumar *et al.* (2017) reported that the induction was smooth and uneventful after dexmedetomidine-propofol and xylazine-propofol combination.

4.2.8 Quality of Anaesthesia (Table 4.3)

Isoflurane was used for maintenance of anaesthesia in all the animals of both groups. Quality of maintenance anaesthesia was evaluated by recording jaw tone, pedal reflex, palpebral reflex and eye ball position at different time intervals.

4.2.8.1 Jaw Tone

Strong jaw tone was observed before administration of preanaesthetic which subsequently abolished completely after induction of anesthesia in all the animals of both groups. Jaws remained open in all the animals with mean score values of 4.00 during entire maintenance period in both the groups.

4.2.8.2 Palpebral Reflex

Quick blinking of eyes in response to touching the skin was observed which completely abolished after induction of anaesthesia and maintained throughout the surgery with mean score of 4.00 in animals of both the groups.

4.2.8.3 Pedal Reflex

Before administration of preanaesthetic, strong withdrawal of limb was observed on pinching the interdigital skin with Allies Tissue Forceps in animals of both groups. After induction of anaesthesia and during maintenance period, pedal reflex remained completely abolished with mean score of 4.00.

4.2.8.4 Eyeball Position

Ventromedial rotation of eyeball without nystagmus was observed after induction of anaesthesia and during maintenance period in all the animals of both the groups.

Mean score values of jaw tone, palpebral reflex, pedal reflex and eyeball position were observed excellent throughout maintenance period without any statistical differences which reflects the excellent quality of maintenance anaesthesia with sufficient depth, muscle relaxation and analgesia during surgery. Various researchers *viz;* (Kussela *et al.*, 2001; Kuusela *et al.*, 2003; Dewangan *et al.*, 2010 and Arunkumar *et al.*, 2017) also found isoflurane produced excellent quality of maintenance anaesthesia with adequate control over depth in their studies and concluded it as safe.

4.2.9 Quality of Recovery (Table 4.2)

Quality of recovery was found excellent with mean score value of 4.00±0.00 in group I and 3.83±0.17 in group II which showed non-significant difference between the groups.

Seliskar *et al.* (2007); Alkattan and Helal (2013); Ferreira *et al.* (2015) and Thejasree *et al.* (2018) reported smooth and uneventful recovery after propofol anaesthesia. Similarly, Grasso *et al.* (2015) and Diao *et al.* (2016) also reported smooth, quick and uneventful recovery in propofol induced and isoflurane-maintained dogs. Kuusela *et al.* (2003) reported recovery that was always smooth in dexmedetomidine-propofol-isoflurane anaesthesia in dogs.

Mukati *et al.* (2006) reported smooth and excitement free recovery in xylazine-propofol anaesthesia. Jena *et al*. (2014) and Arunkumar *et al.* (2017) reported that the recovery was smooth and uneventful after dexmedetomidine-propofol and xylazine-propofol anaesthesia.

4.3 CLINICO-PHYSIOLOGICAL PARAMETERS

The clinico-physiological parameters *viz*; rectal temperature (ºF), pulse rate (beats/minute), systolic blood pressure (mm Hg), diastolic blood pressure (mm Hg), mean arterial pressure (mm Hg) and peripheral saturation of oxygen (%) were recorded before administration of preanaesthetics, prior to induction, after induction of anaesthesia and thereafter at every 10 minutes interval up to 50 minutes using vital signs monitor. The results of which are discussed as under.

4.3.1 Rectal Temperature (Table 4.4; Chart 4.1)

The mean±SE values of rectal temperature (°F) were 101.57±0.57, 100.45±0.58, 99.58±0.55, 99.05±0.47, 98.50±0.28, 97.83±0.27, 97.43±0.24 and 96.70±0.22 in group I and 101.65±0.29, 100.73±0.25, 99.75±0.2, 99.08±0.12, 98.55±0.12, 97.95±0.15, 97.53±0.17 and 96.82±0.14 in group II before administration of preanaesthetic, after preanaesthetic, after induction and thereafter at every 10 minutes interval up to 50 minutes, respectively.

Gradual and highly significant decrease in rectal temperature was observed after induction of anaesthesia in group I and a significant decrease in rectal temperature after administration of xylazine was observed in group II However; non-significant difference was observed between groups at different time intervals.

Lemke (2007) stated that the decrease in rectal temperature recorded after dexmedetomidine administration might be attributed to a possible decrease in heat

production due to sedation and decreased muscular activity and activation of α-2 C receptors by dexmedetomidine contributed to hypothermia.

Jena *et al.* (2014) reported significant decrease in rectal temperature from 15 minutes onwards in dexmedetomidine-propofol anaesthesia and significant decrease at 15 minutes which remained significantly less from 30 minutes until the end of observation period in xylazine-propofol anaesthesia. Arunkumar *et al.* (2017) reported that rectal temperature decreased nonsignificantly in dexmedetomidine and xylazine treated dogs. Aslam *et al.* (2019) reported non-significant decrease in rectal temperature with xylazine-propofol and medetomidine-propofol anaesthesia. Chandrakala *et al.* (2017) reported non-significantly decrease in the rectal temperature at 10,20and 30 min intervals and thereafter, it decreased significantly in comparison to the base line value in tramadol-xylazine-propofol anaesthesia.

Similarly, Congdon *et al.* (2011); Rafee *et al.* (2015); Diao *et al.* (2016) and Mate and Aher (2019) noticed significant decrease in rectal temperature after dexmedetomidine-propofol administration at different time intervals. Sahoo *et al.* (2018) reported a non-significant decrease in rectal temperature from base value after dexmedetomidine administration. Vijay *et al.* (2018) reported significant decrease in rectal temperature in butorphanol-dexmedetomidine-propofol-isoflurane anaesthesia.

4.3.2 Pulse Rate (Table 4.5; Chart 4.2)

The mean±SE values of pulse rate (beats/minute) were 107.33±2.36, 62.33±5.24, 98.17±4.11, 101.17±1.94, 105.00±7.95, 101.33±10.07, 108.00±7.68 and 103.83±6.41 in group I and 106.33±3.24, 64.33±1.61, 97.33±1.41, 106.33±1.41, 108.67±4.2, 107.67±2.19, 106.83±5.11 and 104.83±4 in group II before administration of preanaesthetic, after administration of preanaesthetic, after induction and thereafter at every 10 minutes interval up to 50 minutes, respectively.

Significant decrease in pulse rate was observed after administration of preanaesthetic which gradually and nonsignificantly returned to near base value at 50^{th} minutes within the group, However, non-significant difference in pulse rate was observed between the groups at different time intervals.

Initial decrease in heart rate after dexmedetomidine administration might be due to reflex bradycardia as a result of α-2 agonist induced vasoconstriction as reported by Lemke (2007). Similarly, Kuusela *et al.* (2000) reported 60% to 66% decrease in heart rate after administration of dexmedetomidine @ 10 µg/kg IV. Bloor *et al.* (1992) reported 53% decrease in heart rate after administration of

dexmedetomidine @ 20µg/kg. Congdon *et al.* (2011) observed that heart rate was decreased from 110±14.2 beats/min to 49.4±10.4 beats/min within15 minutes after administration of dexmedetomidine. Kuusela *et al.* (2001); Ahmad *et al.* (2013) and Arunkumar *et al.* (2017) reported significant decrease in heart rate after administration of dexmedetomidine which returned to base values after induction with propofol.

Cassu *et al.* (2014) reported marked reduction in heart rate after xylazine administration, whereas, Dewangan *et al.* (2010) reported significant decrease in heart rate after xylazine-propofol anaesthesia. Aslam *et al.* (2019) reported initial decrease in pulse rate after administration of xylazine due to peripheral vasoconstriction followed by vasodilatation. Jena *et al.* (2014) and Mate and Aher (2019) reported significant decrease in heart rate after xylazine and dexmedetomidine administration to propofol anaesthesia.

4.3.3 Respiration Rate (Table 4.6; Chart 4.3)

The mean±SE values of respiration rate (breaths/minute) were 30.00±0.89, 20.00±1.79, 14.00±0.89, 16.00±1.79, 16.00±1.03, 16.67±1.61, 17.33±1.69 and 16.67±1.61 in group I whereas, in group II these were 30.00±2.63, 17.33±1.33, 14.00±1.71, 15.33±1.23, 15.33±1.23, 16.67±1.61, 16.00±1.79 and 16.67±1.23 in group II before administration of preanaesthetic, after administration of preanaesthetic, after induction and thereafter at every 10 minutes interval up to 50 minutes, respectively.

Kuusela *et al.* (2001); Gomez-Villamandos *et al.* (2006); Jena *et al.* (2014); Diao *et al.* (2016) and Mate and Aher (2019) used propofol as induction of anaesthesia and they reported significant decrease in respiration rate after induction of anaesthesia that remained significantly below base line value till the end of observation period. Jena *et al*. (2014) reported significantly decreased respiration rate at 10 minutes and values remained significantly ($p<0.01$) lower than the base line value in xylazine group and dexmedetomidine group to propofol anaesthesia. Cardoso *et al.* (2014); Kellihan *et al.* (2015) and Nishimura *et al.* (2017) reported significant decrease in respiration rate, when compared with the baseline value, after administration of dexmedetomidine and dexmedetomidine-opioids combinations.

Dewangan *et al.* (2010) and Chandrakala *et al.* (2017) reported significant decrease in respiration rate as compared to baseline in tramadol-xylazine-propofol and xylazine-propofol anaesthesia, respectively. Monteiro *et al.* (2008); Welsh (2009) and

Aslam *et al.* (2019) reported that respiration rate decreased significantly after administration of xylazine. Similarly, Arunkumar *et al.* (2017) also reported significant decrease in respiration rate throughout the study period in xylazine-propofol anaesthesia.

Similarly, in the present study the respiration rate showed highly significant decrease after dexmedetomidine and xylazine administration which remained significantly lower at different time interval as compared to base value in both the groups, however; it showed non-significant difference between the groups.

Contrarily, Sahoo *et al.* (2018) reported respiration rate decrease non-significantly from base value after xylazine administration.

4.3.4 Systolic, Diastolic and Mean Arterial Blood Pressure (Table 4.8)

The mean±SE values of systolic blood pressure (mm of Hg) were 136.83±5.72, 134.00±7.01, 127.17±8.77, 124.83±11.41, 122.83±10.67, 122.00±8.00, 116.17±5.77 and 113.33±4.79 in group I and 135.83±6.93, 128.50±6.63, 123.83±6.28, 123.00±4.79, 122.5±4.25, 121.33±2.93, 118.83±2.39 and 113.33±3.07 in group II **(Chart 4.4)** before administration of preanaesthetic, after administration of preanaesthetic, after induction and thereafter at every 10 minutes interval up to 50 minutes, respectively.

The mean±SE values of diastolic blood pressure (mm of Hg) were 104.83±4.61, 93.5±7.23, 84.67±7.7, 83.83±8.73, 81.50±8.16, 79.50±4.81, 79.00±6.02 and 73.00±3.33 in group I and 103.67±4.22, 89.17±8.86, 80.50±11.46, 88.50±5.89, 82.50±3.16, 77.67±4.84, 77.83±6.41 and 72.17±6.30 in group II **(Chart 4.5)** before administration of preanaesthetic, after administration of preanaesthetic, after induction and thereafter at every 10 minutes interval up to 50 minutes, respectively.

The mean±SE values of mean arterial pressure (mm of Hg) were 115.83±4.83, 108.33±6.45, 103.83±15.86, 97.67±9.95, 82.17±9.12, 78.33±6.92, 85.5±4.33 and 82.83±3.44 in group I and 113.00±4.03, 102.33±8.05, 93.00±10.46, 99.50±5.19, 94.67±3.06, 96.17±3.67, 84.67±6.25 and 86.67±5.35**(Chart 4.6)** in group II before administration of preanaesthetic, after administration of preanaesthetic, after induction and thereafter at every 10 minutes interval up to 50 minutes, respectively.

Non-significant difference was observed in the mean values of systolic blood pressure in group I and significant decrease in group II after 40 minutes of induction. Diastolic blood pressure was significantly reduced after induction in group I and 30 minutes after induction in group II whereas, mean arterial blood pressure showed

significant decrease after 20 minutes of induction in group I and 40 minutes of induction in group II. Blood pressure showed nonsignificant difference between the groups in the present study.

Kuusela *et al.* (2001) and Gomez-villamandos *et al.* (2006) reported progressive decrease in SBP, DBP and MAP in dexmedetomidine-propofol-isoflurane anaesthesia. However, Enouri *et al.* (2008) reported increase in blood pressure after administration of medetomidine and induction with thiopentone sodium but it decreased during maintenance with isoflurane. Similarly, in the present study SBP, DBP and MAP decreased after induction with propofol but return near to base line value during maintenance with isoflurane.

Jena *et al.* (2014) reported significant increase in SBP, DBP and MAP after dexmedetomidine administration which decreased after induction with propofol till the end of observation period. Surbhi *et al.,* (2010) reported that propofol decrease systemic arterial blood pressure due to peripheral vasodilation, direct negative inotropic action and direct decrease of arterial and venous vascular tone. Ahmad *et al.* (2013) reported that Mean Arterial Pressure (MAP) increased significantly initially at the 10 minutes interval which decreased gradually and significantly below the baseline value at 60 minutes after administration of dexmedetomidine.

Congdon *et al.* (2013) reported non-significant difference in the mean arterial pressure, systolic arterial pressure and diastolic arterial pressure than baseline values in dexmedetomidine-propofol-isoflurane anaesthesia. Cardoso *et al.* (2014); Kellihan *et al.* (2015) and Rauser *et al.* (2016) reported decrease in systolic blood pressure after opioids and dexmedetomidine anaesthesia.

Redondo *et al.* (1999) reported that no significant difference was observed in systolic, diastolic and mean arterial pressure in xylazine-propofol-halothane anaesthesia. Ilback and Stalhandske (2003) and Jena *et al.* (2014) reported systolic blood pressure and diastolic blood pressure showed a peak increase for about 5–10 minutes and then decreased below the baseline value after administration of xylazine and xylazine-propofol administration respectively. Monteiro *et al.* (2008) reported non-significant decreased in systolic arterial pressure in xylazine and xylazine-methadone anaesthetized dogs.

4.3.5 Saturation of Peripheral Oxygen (Table 4.7; Chart 4.7)

The mean±SE values of saturation of peripheral oxygen were 97.33±0.49, 95.83±0.6, 95.83±0.95, 95.50±0.85, 95.83±1.25, 95.17±1.22, 95.33±1.05 and

95.83±0.6 in group I and 97.17±0.7, 95.67±1.31, 95.33±0.84, 95.33±0.8, 95.50±1.15, 95.67±1.09, 95.50±0.76 and 95.00±0.86 in group II before preanaesthetics, after administration of preanaesthetic, after induction, thereafter at every 10 minutes interval up to 50 minutes, respectively.

Non-significant difference in SpO_2 was observed at different time interval within the group and between the groups. However, when compared to base value mean values of saturation of peripheral oxygen showed slight decrease up to the end of observation period in both the groups.

Kuusela *et al.* (2001); Gomez-Villamandos *et al.* (2006); Rauser *et al.* (2016) and Micieli *et al.* (2017) reported non-significant difference in SpO_2 within groups and between groups at different time intervals after administration of dexmedetomidine.

Diao *et al.* (2016) reported that SpO_2 decreases nonsignificantly after dexmedetomidine-propofol anaesthesia whereas; Vijay *et al.* (2018) reported increase in SpO_2 values from 5 min up to the end of the observation period in dexmedetomidine-propofol anaesthesia.

Welsh (2009) reported fairly maintained SpO_2 after xylazine administration. Jena *et al.* (2014) reported that SpO_2 remained almost similar or slightly increased at different time intervals in xylazine and dexmedetomidine groups.

4.4 HAEMATOLOGICAL PARAMETERS

4.4.1 Haemoglobin, Packed Cell Volume and Total Erythrocyte Count (Table 4.9)

The mean±SE values of haemoglobin were 10.43±0.28, 10.15±0.31, 9.55±0.18, 9.70±0.18, 9.37±0.22 and 9.1±0.26. in group I. Whereas, in group II these were 10.42±0.50, 10.20±0.66, 9.63±0.67, 9.67±0.65, 9.57±0.56 and 9.03±0.44 **(Chart 4.8)** before administration of preanaesthetic, after administration of preanaesthetic, after induction and thereafter at every 15 minutes interval up to 45 minutes, respectively.

Gradual and significant decrease in mean values of haemoglobin was observed after induction and at 30 and45 minutes after induction as compared to the base value in group I whereas gradual and nonsignificant decrease in mean value of haemoglobin was observed at the end of observation in group II. However, it showed non-significant difference between the groups at different time intervals.

The mean±SE values of packed cell volume were 31.48±0.82, 30.45±0.94, 29.33±0.83, 29.32±0.3, 28.48±0.48 and 27.53±0.75 in group I and 31.43±1.37, 30.12±1.51, 29.63±1.28, 29.28±1.76, 28.62±1.68 and 27.47±1.20 in group II. **(Chart 4.9)** before administration of preanaesthetic, after administration of preanaesthetic, after induction and thereafter at every 15 minutes interval up to 45 minutes, respectively.

Significant decrease in mean value of PCV was observed at 30 and 45 minutes after induction as compared to the base line value in group I and non-significant decrease in mean value of PCV as compared to base line value in group II. However; non-significant difference was observed between the groups.

The mean±SE values of total erythrocyte count were 4.88±0.17, 4.68±0.21, 4.44±0.16, 4.34±0.17, 4.40±0.25 and 4.28±0.29 in group I. Whereas, the mean values of total erythrocyte count in group II were 5.04±0.42, 4.74±0.47, 4.92±0.33, 4.50±0.42, 4.93±0.61 and 4.39±0.43 **(Chart 4.10)** before administration of preanaesthetic, after administration of preanaesthetic, after induction and thereafter at every 15 minutes interval up to 60 minutes, respectively.

Non-significant decrease in mean value of total erythrocyte count was observed within and between the groups at different time intervals.

Skarda and Muir (1996) and Dugdale (2010) reported decreased haemoglobin and pack cell volume after administration of α2-adrenoceptors agent in dogs which occured due to decrease in sympathetic activity after administration of dexmedetomidine and it lead to spleenic pooling of circulatory erythrocytes.

Jena *et al.* (2014) observed that Hb and PCV showed a non-significant increase at 30 min in xylazine-propofol anaesthesia and significant decrease in Hb and non-significant decrease in PCV from the base line value were recorded in dexmedetomidine-propofol anaesthesia at 30 minutes. Similarly, Rafee *et al.* (2015) and Mazumdar *et al.* (2015) reported decrease in haemoglobin, packed cell volume and total erythrocyte count after administration of dexmedetomidine as basal anaesthesia in dogs.

Fani *et al.* (2008) reported that total erythrocyte count, packed cell volume and haemoglobin decreased significantly after epidural administration of xylazine. Dewangan *et al.* (2016) and Chandrakala *et al.* (2017) reported non-significant decrease in haemoglobin, packed cell volume and total erythrocyte count after

xylazine-propofol anaesthesia. Aslam *et al.* (2019) reported non-significant decrease in Hb and TEC after xylazine-propofol and medetomidine-propofol anaesthesia.

4.4.2 Total Leukocyte Count and Differential Leukocyte Count (Table 4.10)

The mean±SE values of total leukocyte count were 13.48±2.31, 13±2.15, 12.90±2.61, 12.08±2.13, 11.23±1.79 and 10.60±2.03 group I and 13.65±2.82, 13.43±2.74, 13.17±2.69, 12.532±2.25, 11.60±1.91 and 10.80±1.72 in group II **(Chart 4.11)** before administration of preanaesthetic, after administration of preanaesthetic, after induction and thereafter at every 15 minutes interval up to 45 minutes, respectively.

There was a gradual and non-significant difference in total leukocyte count was observed at different time interval within the group and between the groups. However, when compared to base line value mean values of total leukocyte count showed non-significant decrease up to end of observation period in both the groups.

The mean±SE values of neutrophils were 67±4.67, 64.17±1.85, 63.67±2.85, 67±2.77, 66.17±4.9 and 66.17±2.41 in group I, whereas; the mean values of neutrophils in group II were 66.67±3.86, 64±2.79, 63.33±2.06, 66±2.44, 67±2.7 and 66±1.63 **(Chart 4.12)** before administration of preanaesthetic, after induction and thereafter at every 15 minutes interval up to 45 minutes, respectively.

When the mean values of neutrophils were compared between groups, non-significant difference was observed at different time intervals. However; it decreased nonsignificantly up to end of observation in both groups as compared to the base values.

The mean±SE value of lymphocytes were 26.17±3.34, 28.17±1.85, 28.67±2.8, 27.33±2.85, 27.83±4.35 and 27.50±2.51 in group I and 26.17±2.43, 27.83±2.50, 28.67±1.36, 27.83±1.82, 26.50±1.96 and 27.33±1.26 in group II **(Chart 4.13)** before administration of preanaesthetic, after administration of preanaesthetic, after induction and thereafter at every 15 minutes interval up to 45 minutes, respectively.

Mean value of lymphocyte increased non-significantly at different time interval still the end of observation period in both the groups. However; no significant difference was observed between the groups.

The mean±SE values of monocytes were 5.67±1.67, 6.67±1.33, 6.17±0.91, 4.83±1.30, 5.00±1.18 and 5.50±1.06 in group I and 6±1.71, 7±1.53, 6.33±0.8, 5±1.21, 5.33±1.43 and 5.67±1.26 in group II **(Chart 4.14)** before administration of

preanaesthetic, after administration of preanaesthetic, after induction and thereafter at every 15 minutes interval up to 45, minutes respectively.

Nonsignificant difference was observed in monocytes count between and within the groups at different time intervals. Mean values of monocytes were increased before and after induction and thereafter it reduced from base line values at 15, 30 and 45 minutes after induction of anaesthesia in both the groups.

The mean±SE values of eosinophils (%) were 1.17±0.31, 1.00±0.26, 1.50±0.43, 0.83±0.31, 1.00±0.26 and 0.83±0.31 in group I and 1.33±0.33, 1.17±0.4, 1.67±0.33, 1.17±0.31, 1.17±0.31 and 1.00±0.37 in group II **(Chart 4.15)** before administration of preanaesthetic, after administration of preanaesthetic, after induction and thereafter at every 15 minutes intervals up to 45 minutes, respectively.

Eosinophil count showed slight increase after induction of anaesthesia which decrease after 30 minutes than base values in both the groups. However, the difference remained nonsignificant within and between the groups.

Mazumdar *et al.* (2015) and Rafee *et al.* (2015) reported decrease in total leukocyte count after administration of dexmedetomidine as basal anaesthesia in dogs which might be due to haemodilution. Jena *et al.* (2014) used propofol for induction after premedication with xylazine/dexmedetomidine and found decrease in total leukocyte count; whereas, Dewangan *et al.* (2016) reported non-significant increase in total leukocyte count after xylazine-propofol anaesthesia. Chandrakala *et al.* (2017) reported that total leucocytic count and differential leucocytic count except lymphocytes exhibited nonsignificant decrease at different intervals in xylazine-propofol anaesthesia. Aslam *et al.* (2019) observed nonsignificant increase in total leucocytes count in xylazine-propofol and medetomidine-propofol anaesthesia.

4.4.3 Blood glucose (Table 4.11; Chart 4.16)

The mean±SE values of blood glucose (mg/dl) were 88.33±4.92, 92.17±6.50, 103.17±6.43, 109.83±5.62, 116.50±8.82 and 120.17±6.18 in group I and 86.83±6.23, 92.50±6.66, 103.33±6.02, 111.17±5.63, 118.67±4.58 and 121.83±4.21 in group II before administration of preanaesthetic, after administration of preanaesthetic, after induction and thereafter at every 15 minutes intervals up to 45 minutes, respectively.

Lin *et al.* (2008); Dugdale (2010); Pypendop *et al.* (2011); Restitutti *et al.* (2012); Mazumdar *et al.* (2015) and Rafee *et al.* (2015) reported increase in blood glucose level after administration of dexmedetomidine.

Jena *et al.* (2014); Khan *et al.* (2014) Dewangan *et al.* (2016) and Chandrakala *et al.* (2017) reported that blood glucose increased significantly after xylazine-propofol anaesthesia. Fani *et al.* (2008) also reported significant increase in serum glucose value after epidural administration of xylazine in dogs.

Similarly, in the present study glucose level increased significantly at 15, 30 and 45 minutes after induction of anaesthesia as compared to base line value till the end of observation period in both the groups. However; between the groups it showed non-significant difference.

Dollery (1991) reported that increase in glucose level was due to activation of α-2 adrenoceptors present in β-cells of pancreatic islets that suppresses insulin release. However, Surbhi *et al.* (2010) stated that low insulin activity caused inhibition of serum glucose utilization that lead to rise in serum glucose level.

4.5 SERUM BIOCHEMICAL PARAMETERS

4.5.1 Total Protein (Table 4.12; Chart 4.17)

The mean±SE values of total protein were 8.51±0.49, 7.97±0.40, 7.33±0.57, 7.13±0.22, 6.49±0.16 and 5.52±0.15 in group I whereas, these were 8.26±0.41, 7.57±0.30, 7.28±0.31, 6.81±0.32, 6.05±0.4 and 5.33±0.2 in group II before preanaesthesia, after administration of preanaesthetic, after induction and thereafter at every 15 minutes interval up to 45 minutes, respectively.

Gradual and significant decrease in mean values of total protein was observed just after induction and thereafter at 15, 30 and 45 minutes after induction in group I and at 15, 30 and 45 minutes after induction in group II. However, non-significant difference was observed between the groups at different time intervals.

Dugdale (2010) reported that decreased in total protein might be due to a shift of fluid into the intravascular space secondary to hyperglycaemia after α-2 agonist administration. Mazumdar *et al.* (2015) reported non-significant decrease in total protein after dexmedetomidine administration; similarly, Dewangan *et al.* (2016) also reported decrease in total protein level after administration of xylazine and propofol in dogs. However total protein decreased significantly in xylazine-ketamine anaesthesia as reported by Çamkerten *et al.* (2013)

4.5.2 Alanine Amino Transferase (Table 4.13; Chart 4.18)

The mean±SE values of ALT were 25.54±1.94, 28.33±2.98, 32.53±2.72, 27.71±2.63, 25.95±1.53 and 20.93±1.81 in group I and 25.07±2.47, 28.67±3.31, 32.25±3.34, 28.19±4.2, 25.36±1.55 and 21.09±1.71 in group II before preanaesthesia,

after administration of preanaesthetic, after induction and thereafter at every 15 minutes intervals up to 45 minutes, respectively. In the present study, no significant difference in the mean values of ALT was observed within and between the groups.

Saini *et al.* (2017) reported increase in alanine amino transferase level after administration of dexmedetomidine in dogs.

Dewangan *et al.* (2016) reported significant increase in ALT up to 35 minutes post anaesthesia which returned to near normal by 60 minutes in xylazine-propofol anaesthesia. Chandrakala *et al.* (2017) also reported consistent increase in ALT at different intervals after administration of butorphanol-xylazine-propofol anaesthesia. Thejasree *et al.* (2018) reported non-significant increase of ALT in propofol anaesthesia. Aslam *et al.* (2019) reported non-significant increase in ALT in xylazine-propofol and medetomidine-propofol anaesthesia.

4.5.3 Blood Urea Nitrogen (Table 4.14; Chart 4.19)

The mean±SE values of blood urea nitrogen were 8.97±1.33, 10.61±1.62, 11.76±1.80, 12.79±1.82, 13.48±1.69 and 15.43±1.77 in group I, whereas in group II there were 9.76±1.67, 10.75±1.87, 11.72±1.97, 12.19±2.35, 13.77±2.39 and 15.19±2.31 before preanaesthesia, after preanaesthetic, after induction and thereafter at every 15 minutes intervals up to 45 minutes, respectively.

Non-significant difference was observed in the mean values of blood urea nitrogen within and between the groups at different time intervals. When compared to base values, mean values of blood urea nitrogen increased non-significantly up to the end of observation period in both groups.

Umar and Adam (2013) reported non-significant changes in BUN after α-2 agonist premedication. Mazumdar *et al.* (2015) reported significant increase in blood urea nitrogen after administration of dexmedetomidine in dogs. Saini *et al.* (2019) reported non-significant increase in BUN after administration of dexmedetomidine in dogs.

Fani *et al.* (2008) and Khan *et al.* (2014) reported significant increase in BUN after xylazine administration. Jena *et al.* (2014) reported that blood urea nitrogen and creatinine showed nonsignificant decrease at 30 min followed by a nonsignificant increase at 60 min in dexmedetomidine-propofol and xylazine-propofol anaesthesia. Aslam *et al.* (2019) also reported non-significant increase in BUN after xylazine-propofol anaesthesia and medetomidine-propofol anaesthesia.

4.5.4 Serum Creatinine (Table 4.15; Chart 4.20)

The mean±SE values of serum creatinine (mg/dl) were 0.98±0.03, 1.10±0.03, 1.19±0.05, 1.30±0.04, 1.32±0.03 and 1.35±0.02 in group I and 0.97±0.04, 1.09±0.03, 1.23±0.02, 1.29±0.06, 1.33±0.05 and 1.38±0.04 in group II before preanaesthesia, after administration of preanaesthetic, after induction and thereafter at every 15 minutes intervals up to 45 minutes, respectively.

There was a significant increased in the mean value of creatinine up to end of observation when compared to base value in both the groups. However, non-significant difference was observed between the groups.

Restitutti *et al.* (2012) reported fluctuations in creatinine value during dexmedetomidine administration might be due to the inhibitory effect of drugs on the renal blood flow, which led to increased creatinine production from muscle damage and amino acid degradation. Mazumdar *et al.* (2015) reported significant increase in creatinine level in the dogs after dexmedetomidine administration. Surbhi *et al.* (2010) reported that creatinine values increased non-significantly after butorphanol-medetomidine-propofol anaesthesia.

Umar and Adam (2013) reported significant increase in creatinine value after α-2 agonist premedication. Fani *et al.* (2008) reported no change in creatinine after epidural administration of xylazine.

Jena *et al.*, (2014) reported that value of creatinine showed a similar pattern in dexmedetomidine-propofol and xylazine-propofol groups, where there was a non-significant decrease at 30 min followed by a non-significant increase at 60 min. Rafee *et al.* (2015) reported non-significant decrease in creatinine values after dexmedetomidine alone. Dewangan *et al.*, (2016); Chandrakala *et al.* (2017) and Aslam *et al.* (2019) reported increase in the value of creatinine during xylazine-propofol anaesthesia.

4.6 Complication

No major complications or adverse effects were observed during entire the study.

Table 4.1 Mean±SE values of induction dose and different anaesthetic time parameters in dogs (n=6 in each group)

GROUPS	Dose of induction anaesthesia (mg/kg)	Duration of maintenance anaesthesia (min.)	Duration of surgery (min.)	Total duration of anaesthesia (min.)	Recovery time (min.)
I	0.90±0.13[a]	65.83±6.32[a]	59.33±5.81[a]	73.17±5.78[a]	4.17±0.65[a]
II	1.29±0.26[a]	71.83±12.49[a]	67.17±11.88[a]	80.33±13.03[a]	4.33±1.09[a]
'P' Value	0.20	0.68	0.57	0.63	0.90

Means bearing same superscripts differ nonsignificantly between the groups ($P \geq 0.05$).

Table 4.2 Mean±SE values of quality for different anaesthetic parameters in dogs (n=6 in each group)

GROUPS	Quality of sedation	Quality of induction	Quality of recovery
I	4±0[a]	4±0[a]	4±0[a]
II	4±0[a]	4±0[a]	4±0[a]
P Value	0.34	0.34	0.34

Means bearing same superscripts differ nonsignificantly between the groups ($P \geq 0.05$).

Table 4.3 Mean±SE score values of different reflexes

Parameter	Groups	0 min	Before Induction	After Induction	10 min after induction	20 min after induction	30 min after induction	40 min after induction	50 min after induction
Jaw tone	**I**	0±0	2.83±0.06	4±0	4±0	4±0	4±0	4±0	4±0
	II	0±0	2.33±0.08	4±0	4±0	4±0	4±0	4±0	4±0
Palpebral reflex	**I**	0±0	2.83±0.06	4±0	4±0	4±0	4±0	4±0	4±0
	II	0±0	2.67±0.09	4±0	4±0	4±0	4±0	4±0	4±0
Pedal reflex	**I**	0±0	2.83±0.07	4±0	4±0	4±0	4±0	4±0	4±0
	II	0±0	2.50±0.09	4±0	4±0	4±0	4±0	4±0	4±0
Eyeball position	**I**	0±0	2.50±0.09	4±0	4±0	4±0	4±0	4±0	4±0
	II	0±0	2.50±0.09	4±0	4±0	4±0	4±0	4±0	4±0

Table 4.4 Mean±SE values of rectal temperature at different time intervals in dogs

	Rectal Temperature (°F)								
Groups	**0 minute**	**Before Induction**	**After Induction**	**10 min after induction**	**20 min after induction**	**30 min after induction**	**40 min after induction**	**50 min after induction**	***P Value***
I	$101.57\pm0.57^{a}{}_{A}$	$100.45\pm0.58^{ab}{}_{A}$	$99.58\pm0.55^{bc}{}_{A}$	$99.05\pm0.47^{cd}{}_{A}$	$98.5\pm0.28^{cde}{}_{A}$	$97.83\pm0.27^{def}{}_{A}$	$97.43\pm0.24^{ef}{}_{A}$	$96.7\pm0.22^{f}{}_{A}$	0.000
II	$101.65\pm0.29^{a}{}_{A}$	$100.73\pm0.25^{b}{}_{A}$	$99.75\pm0.2^{c}{}_{A}$	$99.08\pm0.12^{d}{}_{A}$	$98.55\pm0.12^{d}{}_{A}$	$97.95\pm0.15^{e}{}_{A}$	$97.53\pm0.17^{e}{}_{A}$	$96.82\pm0.14^{f}{}_{A}$	0.000
P Value	0.899	0.664	0.782	0.947	0.872	0.714	0.745	0.665	

Means bearing different superscripts differ significantly within the group ($P \leq 0.05$).
Means bearing same subscripts differ nonsignificantly between the groups ($P > 0.05$).

Table 4.5 Mean±SE values of pulse rate at different time intervals in dogs

	Pulse Rate (beats/minute)								
Groups	**0 minute**	**Before Induction**	**After Induction**	**10 min after induction**	**20 min after induction**	**30 min after induction**	**40 min after induction**	**50 min after induction**	***P Value***
I	$107.33\pm2.36^{a}{}_{A}$	$62.33\pm5.24^{b}{}_{A}$	$98.17\pm4.11^{a}{}_{A}$	$101.17\pm1.94^{a}{}_{A}$	$105\pm7.95^{a}{}_{A}$	$101.33\pm10.07^{a}{}_{A}$	$108\pm7.68^{a}{}_{A}$	$103.83\pm6.41^{a}{}_{A}$	0.0001
II	$106.33\pm3.24^{ab}{}_{A}$	$64.33\pm1.61^{c}{}_{A}$	$97.33\pm1.41^{b}{}_{A}$	$106.33\pm1.41^{ab}{}_{A}$	$108.67\pm4.2^{a}{}_{A}$	$107.67\pm2.19^{a}{}_{A}$	$106.83\pm5.11^{ab}{}_{A}$	$104.83\pm4^{ab}{}_{A}$	0.0001
P Value	0.81	0.72	0.85	0.08	0.69	0.55	0.90	0.9	

Means bearing different superscripts differ significantly within the group ($P \leq 0.05$).
Means bearing same subscripts differ nonsignificantly between the groups ($P > 0.05$).

Table 4.6 Mean±SE value of respiration rate at different time intervals in dogs

	Respiratory Rate (breaths/minute)								
Groups	**0 min**	**Before Induction**	**After Induction**	**10 min after induction**	**20 min after induction**	**30 min after induction**	**40 min after induction**	**50 min after induction**	***P Value***
I	$30\pm0.89^{a}{}_{A}$	$20\pm1.79^{b}{}_{A}$	$14\pm0.89^{c}{}_{A}$	$16\pm1.79^{bc}{}_{A}$	$16\pm1.03^{bc}{}_{A}$	$16.67\pm1.61^{bc}{}_{A}$	$17.33\pm1.69^{bc}{}_{A}$	$16.67\pm1.61^{bc}{}_{A}$	0.0001
II	$30\pm2.63^{a}{}_{A}$	$17.33\pm1.33^{b}{}_{A}$	$14\pm1.71^{b}{}_{A}$	$15.33\pm1.23^{b}{}_{A}$	$15.33\pm1.23^{b}{}_{A}$	$16.67\pm1.61^{b}{}_{A}$	$16\pm1.79^{b}{}_{A}$	$16.67\pm1.23^{b}{}_{A}$	0.0001
P Value	1	0.26	1	0.77	0.69	1	0.6	1	

Means bearing different superscripts differ significantly within the group ($P \leq 0.05$).
Means bearing same subscripts differ nonsignificantly between the groups ($P > 0.05$).

Table 4.7Mean±SE values of saturation percentage of oxygen at different time intervals in dogs

	S_PO_2 (%)								
Groups	**0 min**	**Before Induction**	**After Induction**	**10 min after induction**	**20 min after induction**	**30 min after induction**	**40 min after induction**	**50 min after induction**	***P Value***
I	$97.33\pm0.49^{a}{}_{A}$	$95.83\pm0.6^{a}{}_{A}$	$95.83\pm0.95^{a}{}_{A}$	$95.5\pm0.85^{a}{}_{A}$	$95.83\pm1.25^{a}{}_{A}$	$95.17\pm1.22^{a}{}_{A}$	$95.33\pm1.05^{a}{}_{A}$	$95.83\pm0.6^{a}{}_{A}$	0.82
II	$97.17\pm0.7^{a}{}_{A}$	$95.67\pm1.31^{a}{}_{A}$	$95.33\pm0.84^{a}{}_{A}$	$95.33\pm0.8^{a}{}_{A}$	$95.5\pm1.15^{a}{}_{A}$	$95.67\pm1.09^{a}{}_{A}$	$95.5\pm0.76^{a}{}_{A}$	$95\pm0.86^{a}{}_{A}$	0.86
P Value	0.85	0.91	0.7	0.9	0.84	0.76	0.9	0.44	

Means bearing same superscripts differ nonsignificantly within the group ($P > 0.05$).
Means bearing same subscripts differ nonsignificantly between the groups ($P > 0.05$).

Table 4.8 Mean±SE values of systolic, diastolic and mean arterial blood pressure at different time intervals in dogs

Parameter	Groups	0 min	Before Induction	After Induction	10 min after induction	20 min after induction	30 min after induction	40 min after induction	50 min after induction	*P Value*
Systolic blood pressure (mm Hg)	I	$136.83\pm5.72^{a}{}_{A}$	$134\pm7.01^{a}{}_{A}$	$127.17\pm8.77^{a}{}_{A}$	$124.83\pm11.41^{a}{}_{A}$	$122.83\pm10.67^{a}{}_{A}$	$122\pm8^{a}{}_{A}$	$116.17\pm5.77^{a}{}_{A}$	$113.33\pm4.79^{a}{}_{A}$	**0.45**
	II	$135.83\pm6.93^{a}{}_{A}$	$128.5\pm6.63^{ab}{}_{A}$	$123.83\pm6.28^{ab}{}_{A}$	$123\pm4.79^{ab}{}_{A}$	$122.5\pm4.25^{ab}{}_{A}$	$121.33\pm2.93^{ab}{}_{A}$	$118.83\pm2.39^{b}{}_{A}$	$113.33\pm3.07^{b}{}_{A}$	**0.11**
	P Value	**0.91**	**0.58**	**0.76**	**0.89**	**0.98**	**0.94**	**0.68**	**1**	
Diastolic blood pressure (mm Hg)	I	$104.83\pm4.61^{a}{}_{A}$	$93.5\pm7.23^{ab}{}_{A}$	$84.67\pm7.7^{b}{}_{A}$	$83.83\pm8.73^{b}{}_{A}$	$81.5\pm8.16^{b}{}_{A}$	$79.5\pm4.81^{b}{}_{A}$	$79\pm6.02^{b}{}_{A}$	$73\pm3.33^{b}{}_{A}$	**0.05**
	II	$103.67\pm4.22^{a}{}_{A}$	$89.17\pm8.86^{ab}{}_{A}$	$80.5\pm11.46^{b}{}_{A}$	$88.5\pm5.89^{ab}{}_{A}$	$82.5\pm3.16^{ab}{}_{A}$	$77.67\pm4.84^{b}{}_{A}$	$77.83\pm6.41^{b}{}_{A}$	$72.17\pm6.3^{b}{}_{A}$	**0.08**
	P Value	**0.86**	**0.71**	**0.77**	**0.67**	**0.91**	**0.79**	**0.89**	**0.9**	
Mean arterial pressure (mm Hg)	I	$115.83\pm4.83^{a}{}_{A}$	$108.33\pm6.45^{ab}{}_{A}$	$103.83\pm15.86^{abc}{}_{A}$	$97.67\pm9.95^{abc}{}_{A}$	$82.17\pm9.12^{bc}{}_{A}$	$99.33\pm6.92^{c}{}_{A}$	$85.5\pm4.33^{bc}{}_{A}$	$82.83\pm3.44^{bc}{}_{A}$	**0.02**
	II	$113\pm4.03^{a}{}_{A}$	$102.33\pm8.05^{ab}{}_{A}$	$93\pm10.46^{b}{}_{A}$	$99.5\pm5.19^{ab}{}_{A}$	$94.67\pm3.06^{ab}{}_{A}$	$96.17\pm3.67^{ab}{}_{A}$	$84.67\pm6.25^{b}{}_{A}$	$86.67\pm5.35^{b}{}_{A}$	**0.07**
	P Value	**0.66**	**0.57**	**0.58**	**0.87**	**0.22**	**0.72**	**0.91**	**0.56**	

Means bearing different superscripts differ significantly within the group ($P \leq 0.05$).
Means bearing same superscripts differ nonsignificantly within the group ($P > 0.05$).
Means bearing same subscripts differ nonsignificantly between the groups ($P > 0.05$).

Table 4.9Mean±SE values of Hb, PVC and TEC at different time intervals in dogs

Parameter	Groups	Before Preanaesthetic	Before Induction	After induction	15 min after induction	30 min after induction	45 min after induction	*P Value*
Haemoglobin (g%)	**I**	$10.43\pm0.28^{a}{}_{A}$	$10.15\pm0.31^{ab}{}_{A}$	$9.55\pm0.18^{bc}{}_{A}$	$9.7\pm0.18^{abc}{}_{A}$	$9.37\pm0.22^{c}{}_{A}$	$9.1\pm0.26^{c}{}_{A}$	0.005**
	II	$10.42\pm0.5^{a}{}_{A}$	$10.2\pm0.66^{a}{}_{A}$	$9.63\pm0.67^{a}{}_{A}$	$9.67\pm0.65^{a}{}_{A}$	$9.57\pm0.56^{a}{}_{A}$	$9.03\pm0.44^{a}{}_{A}$	0.62
	P Value	0.98	0.95	0.91	0.96	0.75	0.9	
Packed Cell Volume (%)	**I**	$31.48\pm0.82^{a}{}_{A}$	$30.45\pm0.94^{ab}{}_{A}$	$29.33\pm0.83^{abc}{}_{A}$	$29.32\pm0.3^{abc}{}_{A}$	$28.48\pm0.48^{bc}{}_{A}$	$27.53\pm0.75^{c}{}_{A}$	0.009
	II	$31.43\pm1.37^{a}{}_{A}$	$30.12\pm1.51^{a}{}_{A}$	$29.63\pm1.28^{a}{}_{A}$	$29.28\pm1.76^{a}{}_{A}$	$28.62\pm1.68^{a}{}_{A}$	$27.47\pm1.2^{a}{}_{A}$	0.54
	P Value	0.98	0.85	0.85	0.985	0.94	0.96	
Total Erythrocyte Count (million/cu.mm)	**I**	$4.88\pm0.17^{a}{}_{A}$	$4.68\pm0.21^{a}{}_{A}$	$4.44\pm0.16^{a}{}_{A}$	$4.34\pm0.17^{a}{}_{A}$	$4.4\pm0.25^{a}{}_{A}$	$4.28\pm0.29^{a}{}_{A}$	0.35
	II	$5.04\pm0.42^{a}{}_{A}$	$4.74\pm0.47^{a}{}_{A}$	$4.92\pm0.33^{a}{}_{A}$	$4.5\pm0.42^{a}{}_{A}$	$4.93\pm0.61^{a}{}_{A}$	$4.39\pm0.43^{a}{}_{A}$	0.89
	P Value	0.73	0.91	0.21	0.73	0.44	0.84	

Means bearing different superscripts differ significantly within the group ($P \leq 0.05$).
Means bearing same superscripts differ nonsignificantly within the group ($P > 0.05$).
Means bearing same subscripts differ nonsignificantly between the groups ($P > 0.05$).

Table 4.10 Mean±SE values of TLC and DLC at different time intervals in dogs (n=6 in each group)

PARAMETER	GROUPS	Before Preanaesthetic	Before Induction	After induction	15 min after induction	30 min after induction	45 min after induction	*P Value*
Total Leukocyte Count (thousand/cu. mm)	**I**	$13.48\pm2.31^{a}_{A}$	$13\pm2.15^{a}_{A}$	$12.9\pm2.61^{a}_{A}$	$12.08\pm2.13^{a}_{A}$	$11.23\pm1.79^{a}_{A}$	$10.6\pm2.03^{a}_{A}$	0.93
	II	$13.65\pm2.82^{a}_{A}$	$13.43\pm2.74^{a}_{A}$	$13.17\pm2.69^{a}_{A}$	$12.53\pm2.25^{a}_{A}$	$11.6\pm1.91^{a}_{A}$	$10.8\pm1.72^{a}_{A}$	0.95
	P Value	0.96	0.9	0.94	0.89	0.89	0.94	
Neutrophils (%)	**I**	$67\pm4.67^{a}_{A}$	$64.17\pm1.85^{a}_{A}$	$63.67\pm2.85^{a}_{A}$	$67\pm2.77^{a}_{A}$	$66.17\pm4.9^{a}_{A}$	$66.17\pm2.41^{a}_{A}$	0.97
	II	$66.67\pm3.86^{a}_{A}$	$64\pm2.79^{a}_{A}$	$63.33\pm2.06^{a}_{A}$	$66\pm2.44^{a}_{A}$	$67\pm2.7^{a}_{A}$	$66\pm1.63^{a}_{A}$	0.90
	P Value	0.96	0.96	0.93	0.79	0.88	0.96	
Lymphocytes (%)	**I**	$26.17\pm3.34^{a}_{A}$	$28.17\pm1.85^{a}_{A}$	$28.67\pm2.8^{a}_{A}$	$27.33\pm2.85^{a}_{A}$	$27.83\pm4.35^{a}_{A}$	$27.5\pm2.51^{a}_{A}$	0.99
	II	$26.17\pm2.43^{a}_{A}$	$27.83\pm2.5^{a}_{A}$	$28.67\pm1.36^{a}_{A}$	$27.83\pm1.82^{a}_{A}$	$26.5\pm1.96^{a}_{A}$	$27.33\pm1.26^{a}_{A}$	0.95
	P Value	1	0.92	1	0.89	0.79	0.95	
Monocytes (%)	**I**	$5.67\pm1.67^{a}_{A}$	$6.67\pm1.33^{a}_{A}$	$6.17\pm0.91^{a}_{A}$	$4.83\pm1.3^{a}_{A}$	$5\pm1.18^{a}_{A}$	$5.5\pm1.06^{a}_{A}$	0.91
	II	$6\pm1.71^{a}_{A}$	$7\pm1.53^{a}_{A}$	$6.33\pm0.8^{a}_{A}$	$5\pm1.21^{a}_{A}$	$5.33\pm1.43^{a}_{A}$	$5.67\pm1.26^{a}_{A}$	0.92
	P Value	0.89	0.87	0.89	0.92	0.86	0.92	
Eosinophils (%)	**I**	$1.17\pm0.31^{a}_{A}$	$1\pm0.26^{a}_{A}$	$1.5\pm0.43^{a}_{A}$	$0.83\pm0.31^{a}_{A}$	$1\pm0.26^{a}_{A}$	$0.83\pm0.31^{a}_{A}$	0.68
	II	$1.33\pm0.33^{a}_{A}$	$1.17\pm0.4^{a}_{A}$	$1.67\pm0.33^{a}_{A}$	$1.17\pm0.31^{a}_{A}$	$1.17\pm0.31^{a}_{A}$	$1\pm0.37^{a}_{A}$	0.81
	P Value	0.72	0.73	0.77	0.46	0.67	0.73	

Means bearing same superscripts differ nonsignificantly within the group ($P > 0.05$).
Means bearing same subscripts differ nonsignificantly between the groups ($P > 0.05$).

Table 4.11 Mean±SE value of blood glucose at different time intervals in dogs (n=6 in each group)

GROUP	Blood Glucose (mg/dl)						
	Before Preanaesthetic	**Before Induction**	**After induction**	**15 min after induction**	**30 min after induction**	**45 min after induction**	***P Value***
I	$88.33\pm4.92^{c}_{A}$	$92.17\pm6.5^{bc}_{A}$	$103.17\pm6.43^{abc}_{A}$	$109.83\pm5.62^{ab}_{A}$	$116.5\pm8.82^{a}_{A}$	$120.17\pm6.18^{a}_{A}$	0.008
II	$86.83\pm6.23^{c}_{A}$	$92.5\pm6.66^{c}_{A}$	$103.33\pm6.02^{bc}_{A}$	$111.17\pm5.63^{ab}_{A}$	$118.67\pm4.58^{ab}_{A}$	$121.83\pm4.21^{a}_{A}$	0.0004
P Value	0.85	0.97	0.99	0.87	0.83	0.83	

Means bearing different superscripts differ significantly within the group ($P \leq 0.05$).
Means bearing same subscripts differ nonsignificantly between the groups ($P > 0.05$).

Table 4.12 Mean±SE value of total protein at different time intervals in dogs (n=6 in each group)

GROUP	Total Protein (g/dl)						
	Before Preanaesthetic	**Before Induction**	**After induction**	**15 min after induction**	**30 min after induction**	**45 min after induction**	***P Value***
I	$8.51\pm0.49^{a}_{A}$	$7.97\pm0.4^{ab}_{A}$	$7.33\pm0.57^{bc}_{A}$	$7.13\pm0.22^{bc}_{A}$	$6.49\pm0.16^{cd}_{A}$	$5.52\pm0.15^{d}_{A}$	0.0001
II	$8.26\pm0.41^{a}_{A}$	$7.57\pm0.3^{ab}_{A}$	$7.28\pm0.31^{ab}_{A}$	$6.81\pm0.32^{bc}_{A}$	$6.05\pm0.4^{cd}_{A}$	$5.33\pm0.2^{d}_{A}$	0.0001
P Value	0.71	0.44	0.93	0.42	0.33	0.47	

Means bearing different superscripts differ significantly within the group ($P \leq 0.05$).
Means bearing same subscripts differ nonsignificantly between the groups ($P > 0.05$).

Table 4.13 Mean±SE value of ALT at different time intervals in dogs (n=6 in each group)

GROUP	Alanine Amino Transferase (IU/L)						
	Before Preanaesthetic	**Before Induction**	**After induction**	**15 min after induction**	**30 min after induction**	**45 min after induction**	***P Value***
I	$25.54\pm1.94^{ab}{}_{A}$	$28.33\pm2.98^{ab}{}_{A}$	$32.53\pm2.72^{a}{}_{A}$	$27.71\pm2.63^{ab}{}_{A}$	$25.95\pm1.53^{ab}{}_{A}$	$20.93\pm1.81^{b}{}_{A}$	0.40
II	$25.07\pm2.47^{ab}{}_{A}$	$28.67\pm3.31^{ab}{}_{A}$	$32.25\pm3.34^{a}{}_{A}$	$28.19\pm4.2^{ab}{}_{A}$	$25.36\pm1.55^{ab}{}_{A}$	$21.09\pm1.71^{b}{}_{A}$	0.16
P Value	0.88	0.94	0.95	0.93	0.79	0.95	

Means bearing same superscripts differ nonsignificantly within the group (P > 0.05).
Means bearing same subscripts differ nonsignificantly between the groups (P > 0.05).

Table 4.14 Mean±SE value of BUN at different time intervals in dogs (n=6 in each group)

GROUP	Blood Urea Nitrogen (mg/dl)						
	Before Preanaesthetic	**Before Induction**	**After induction**	**15 min after induction**	**30 min after induction**	**45 min after induction**	***P Value***
I	$8.97\pm1.33^{b}{}_{A}$	$10.61\pm1.62^{ab}{}_{A}$	$11.76\pm1.8^{ab}{}_{A}$	$12.79\pm1.82^{ab}{}_{A}$	$13.48\pm1.69^{ab}{}_{A}$	$15.43\pm1.77^{a}{}_{A}$	0.01
II	$9.76\pm1.67^{a}{}_{A}$	$10.75\pm1.87^{a}{}_{A}$	$11.72\pm1.97^{a}{}_{A}$	$12.19\pm2.35^{a}{}_{A}$	$13.77\pm2.39^{a}{}_{A}$	$15.19\pm2.31^{a}{}_{A}$	0.50
P Value	0.72	0.96	0.99	0.85	0.92	0.93	

Means bearing different superscripts differ significantly within the group (P ≤ 0.05).
Means bearing same superscripts differ nonsignificantly within the group (P > 0.05).
Means bearing same subscripts differ nonsignificantly between the groups (P > 0.05).

Table 4.15 Mean±SE value of creatinine at different time intervals in dogs (n=6 in each group)

GROUP	Creatinine (mg/dl)						
	Before Preanaesthetic	**Before Induction**	**After induction**	**15 min after induction**	**30 min after induction**	**45 min after induction**	***P Value***
I	$0.98\pm0.03^{c}_{A}$	$1.1\pm0.03^{b}_{A}$	$1.19\pm0.05^{b}_{A}$	$1.3\pm0.04^{a}_{A}$	$1.32\pm0.03^{a}_{A}$	$1.35\pm0.02^{a}_{A}$	0.0001
II	$0.97\pm0.04^{c}_{A}$	$1.09\pm0.03^{c}_{A}$	$1.23\pm0.02^{b}_{A}$	$1.29\pm0.06^{ab}_{A}$	$1.33\pm0.05^{ab}_{A}$	$1.38\pm0.04^{a}_{A}$	0.0001
P Value	0.98	0.91	0.46	0.94	0.91	0.47	

Means bearing different superscripts differ significantly within the group ($P \leq 0.05$).
Means bearing same subscripts differ nonsignificantly between the groups ($P > 0.05$).

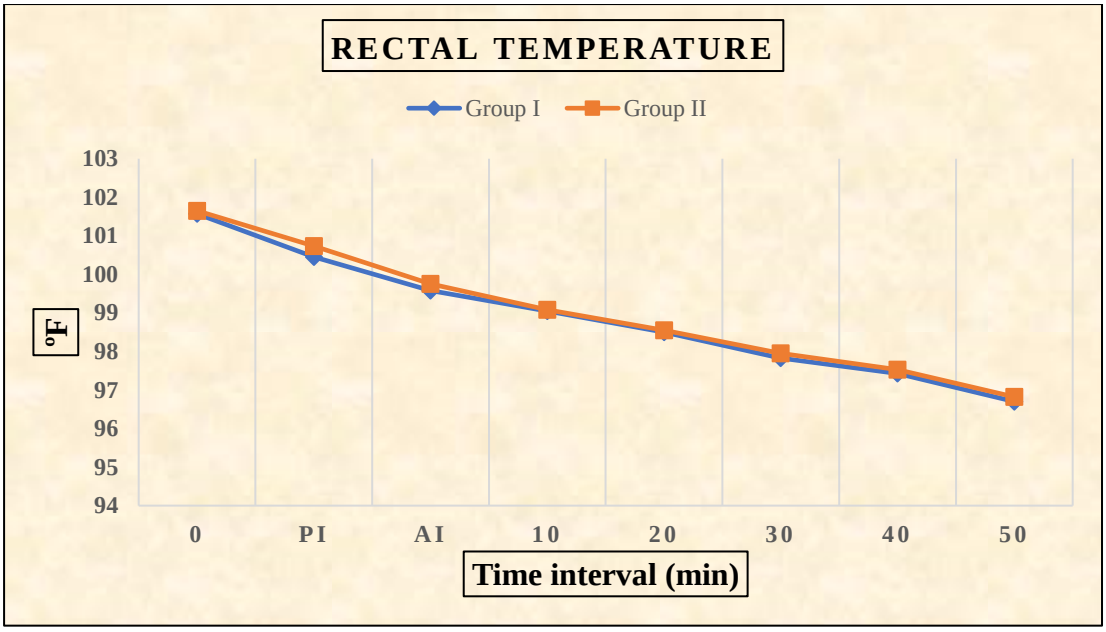

Chart 4.1 Mean values of rectal temperature at different time intervals

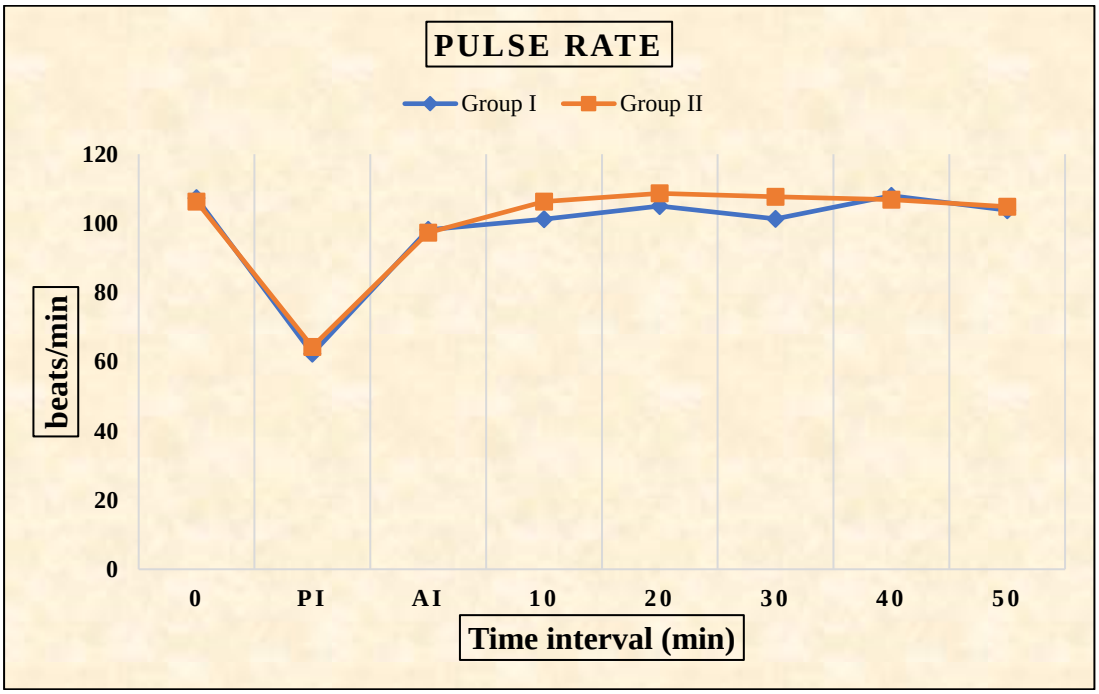

Chart 4.2 Mean values of pulse rate at different time intervals

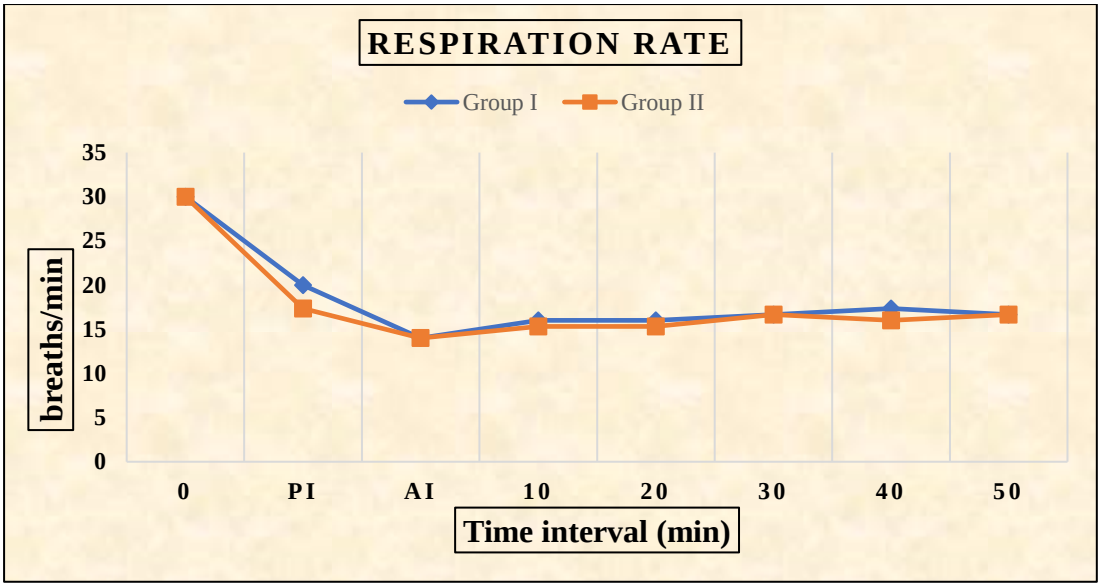

Chart 4.3 Mean values of respiration rate at different time intervals

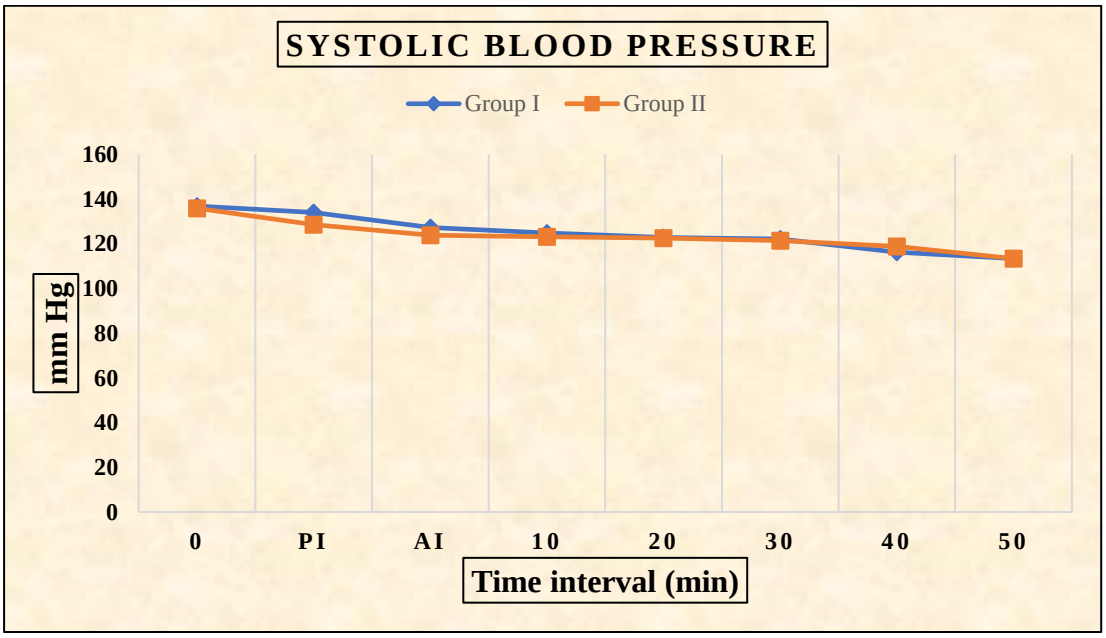

Chart 4.4 Mean values of SBP at different time intervals

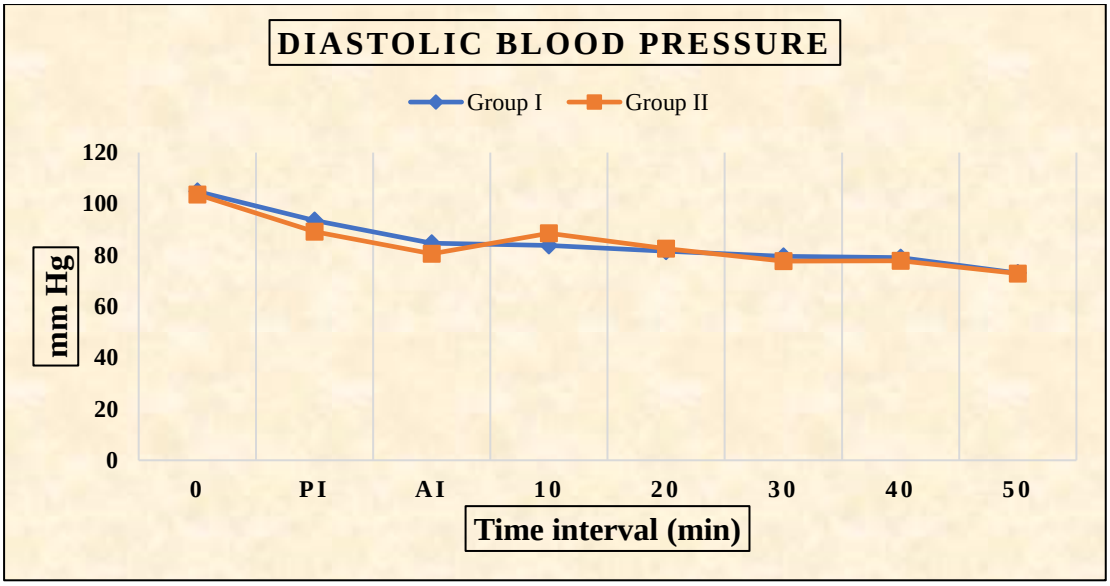

Chart 4.5 Mean values of DBP at different time intervals

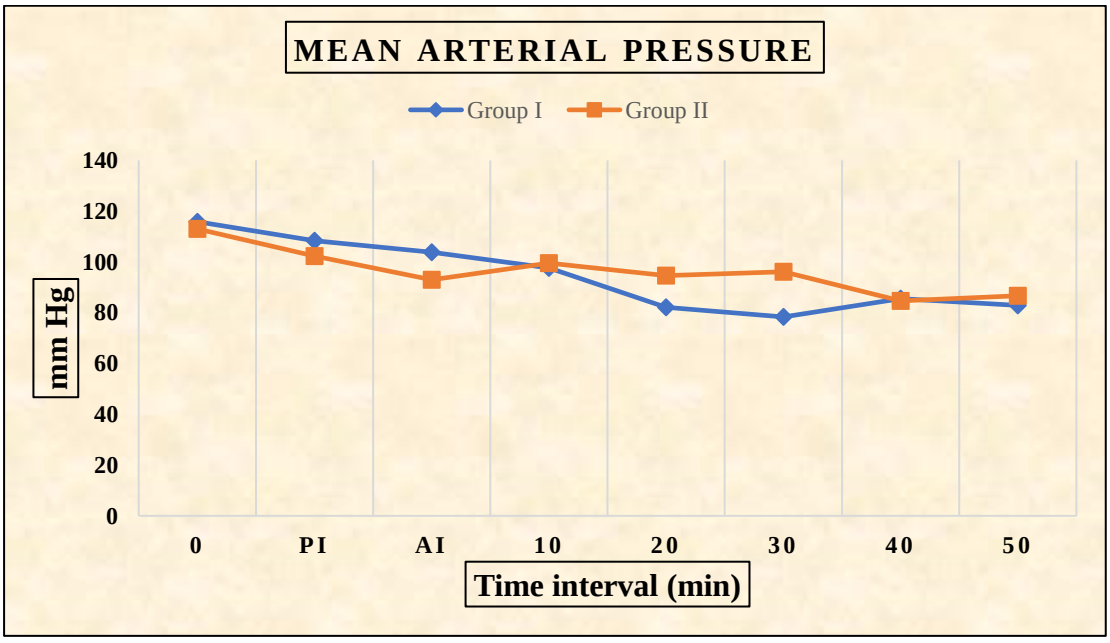

Chart 4.6 Mean values of MAP at different time intervals

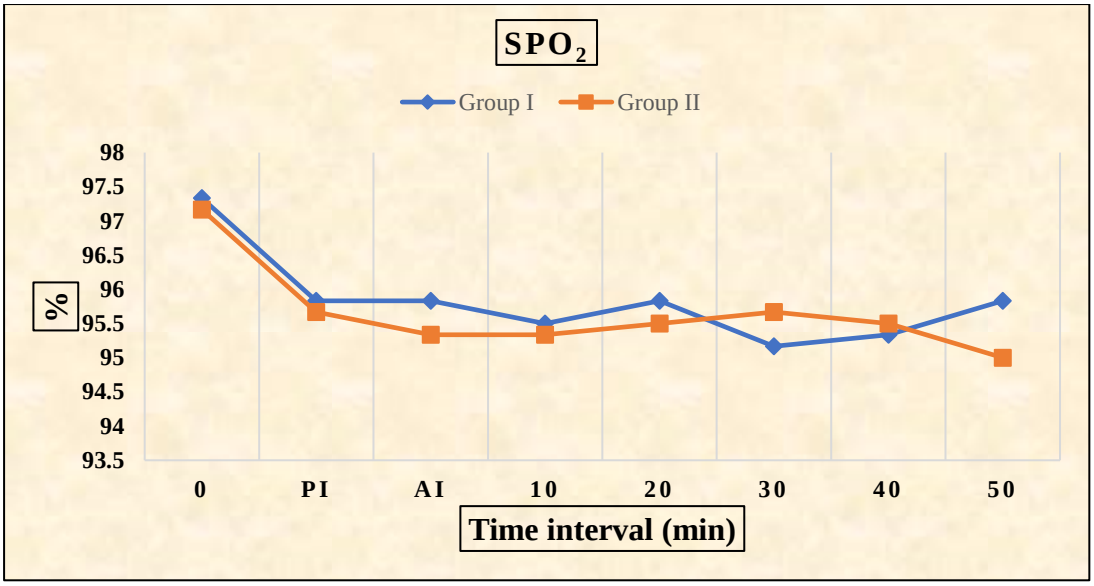

Chart 4.7 Mean values of SpO_2at different time intervals

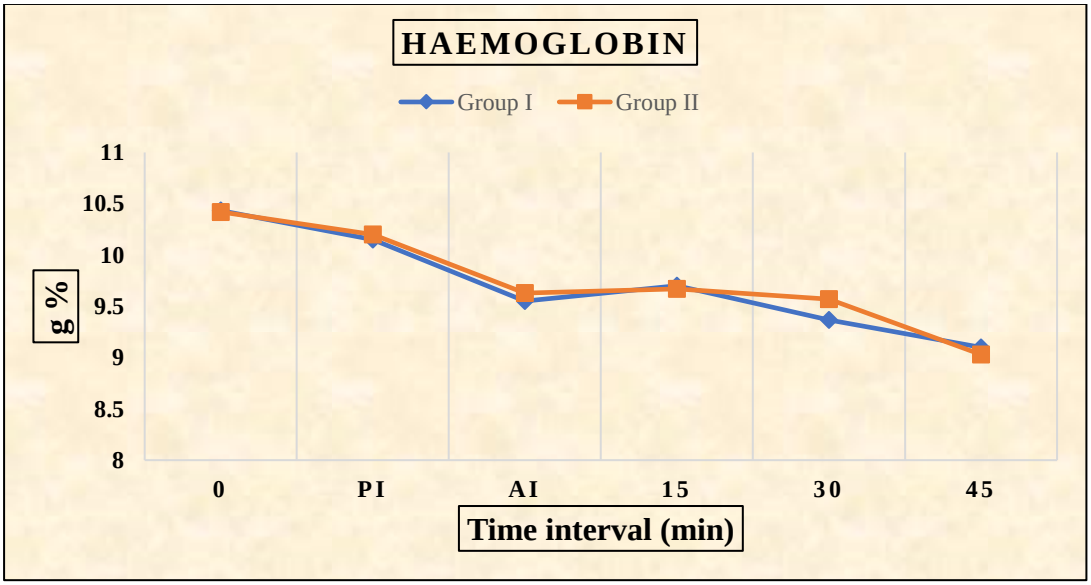

Chart 4.8 Mean values of Hb at different time intervals

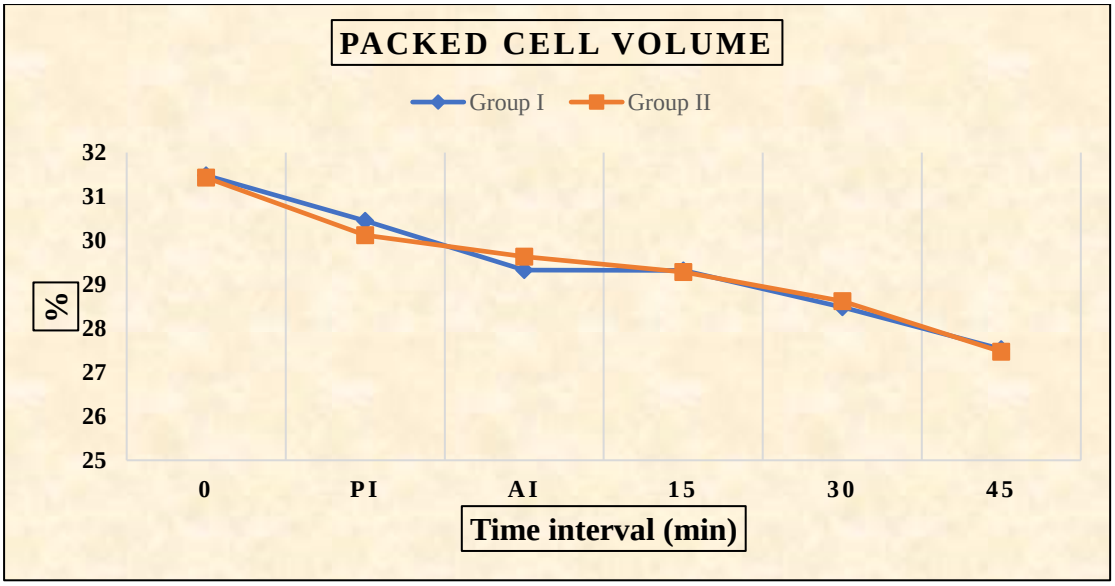

Chart 4.9 Mean values of PCV at different time intervals

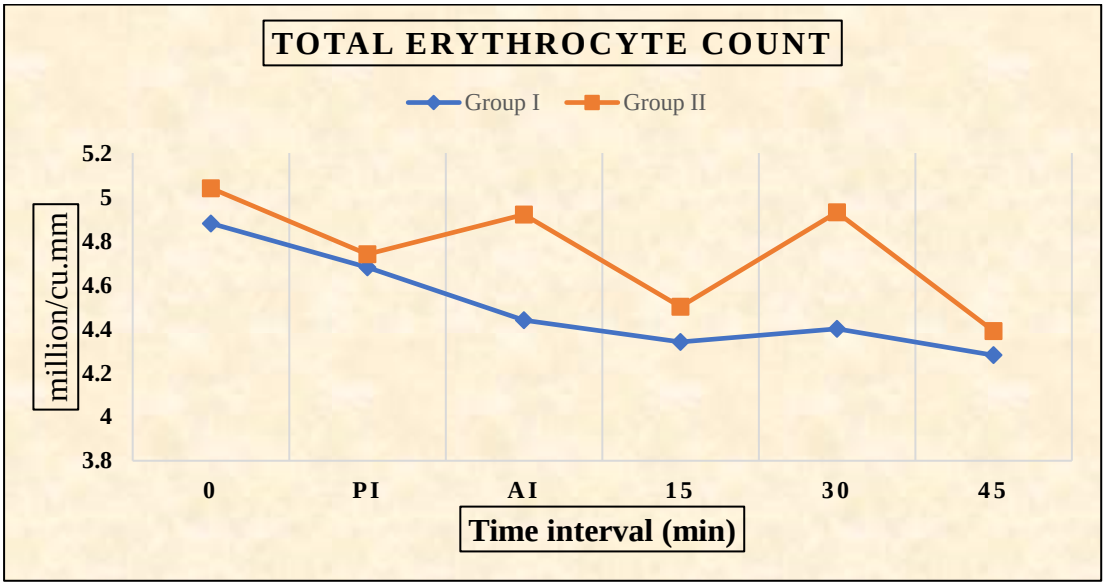

Chart 4.10 Mean values of TEC at different time intervals

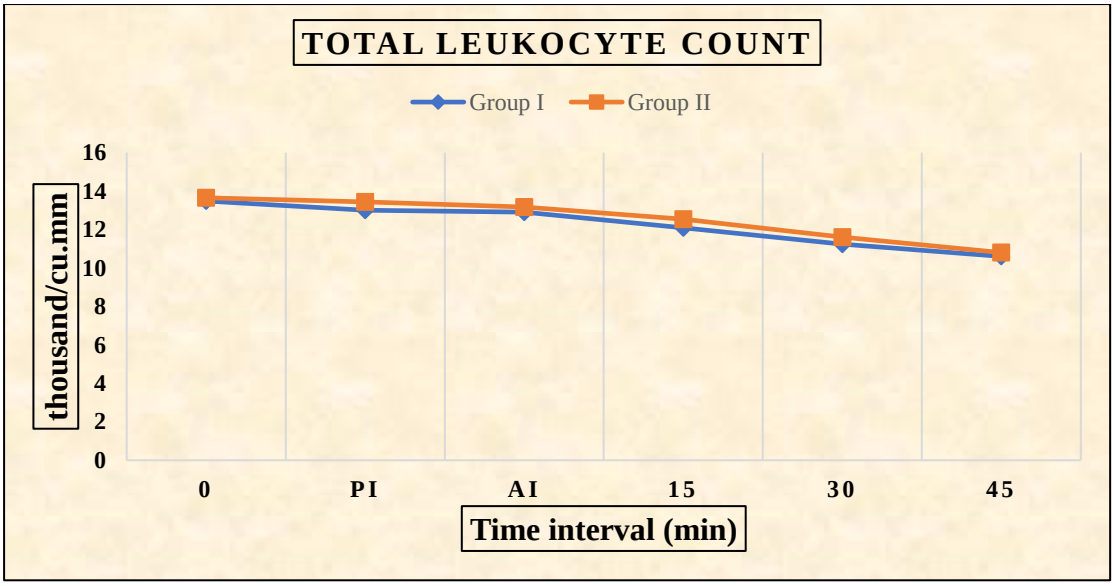

Chart 4.11 Mean values of TLC at different time intervals

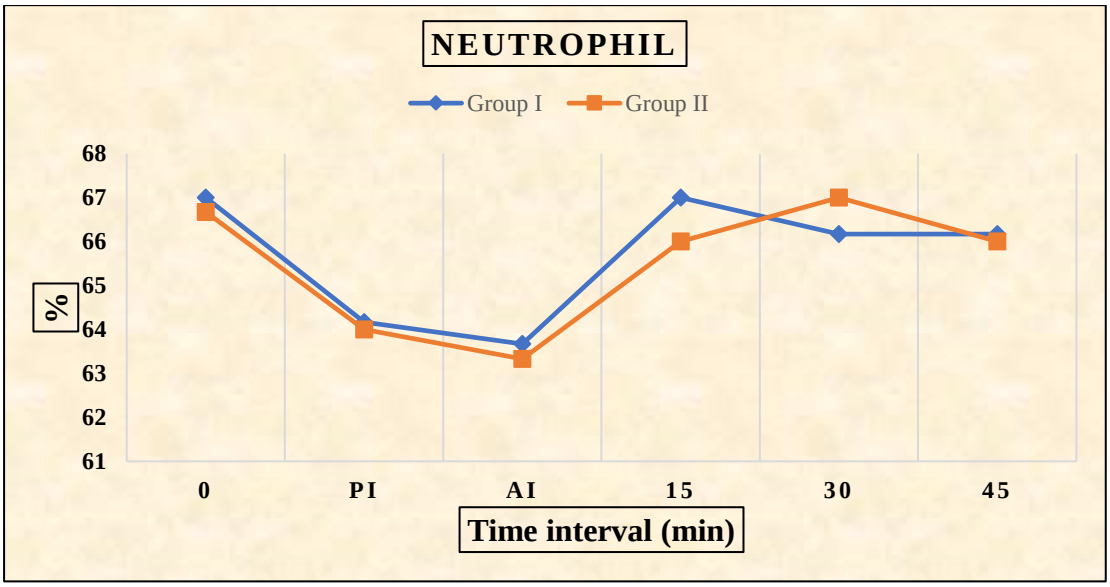

Chart 4.12 Mean values of neutrophil counts at different time intervals

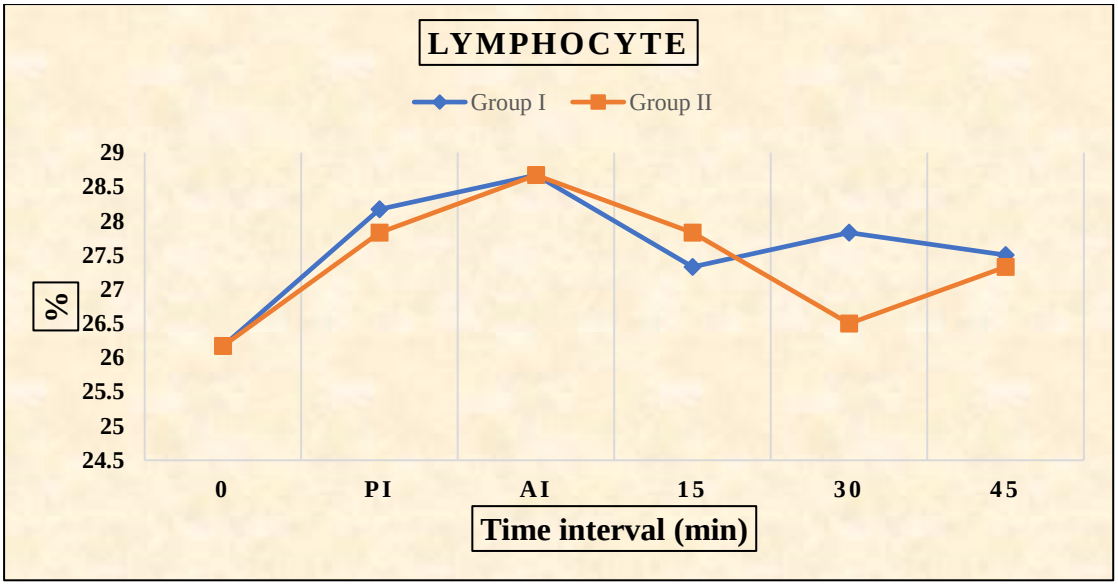

Chart 4.13 Mean values of lymphocyte counts at different time intervals

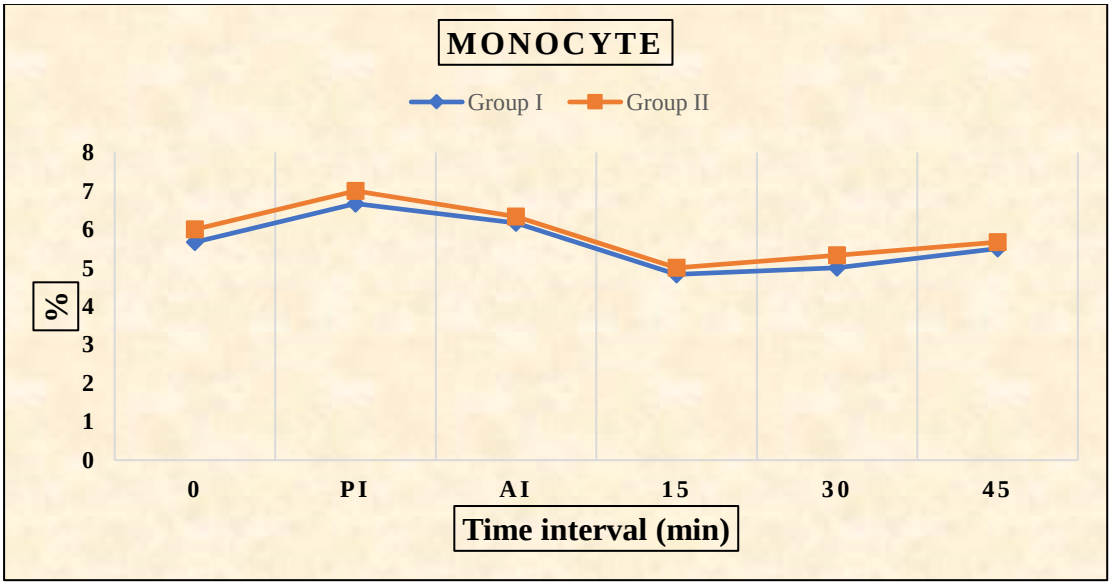

Chart 4.14 Mean values of monocyte counts at different time intervals

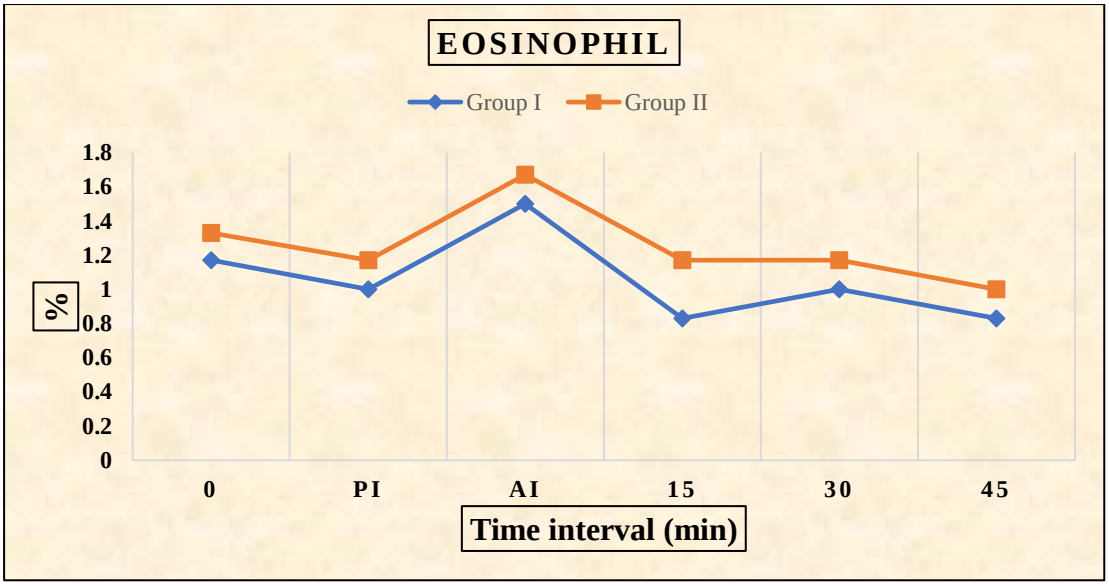

Chart 4.15 Mean values of eosinophil counts at different time intervals

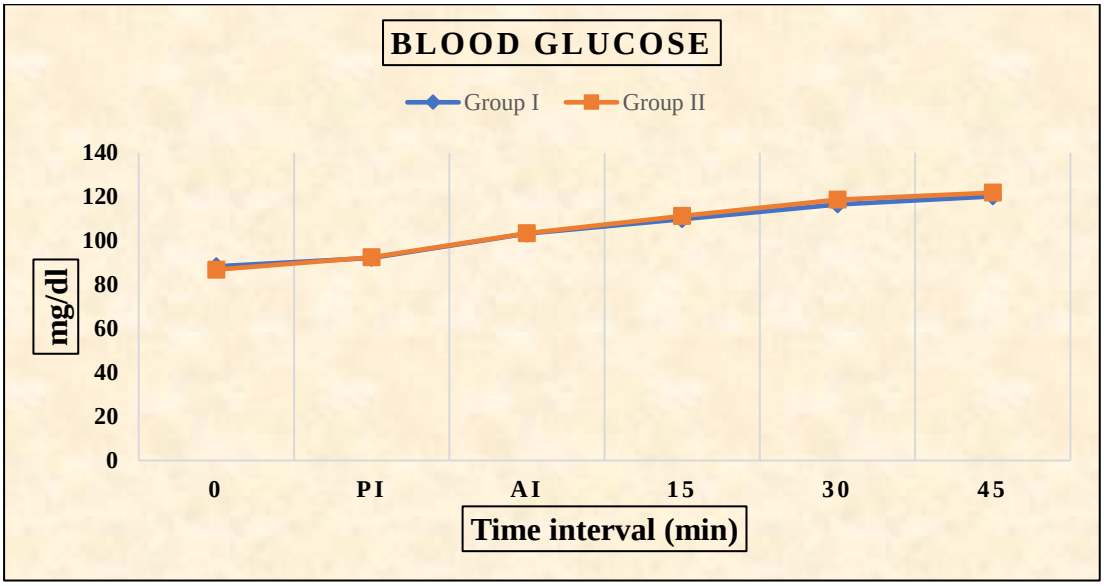

Chart 4.16 Mean values of blood glucose at different time intervals

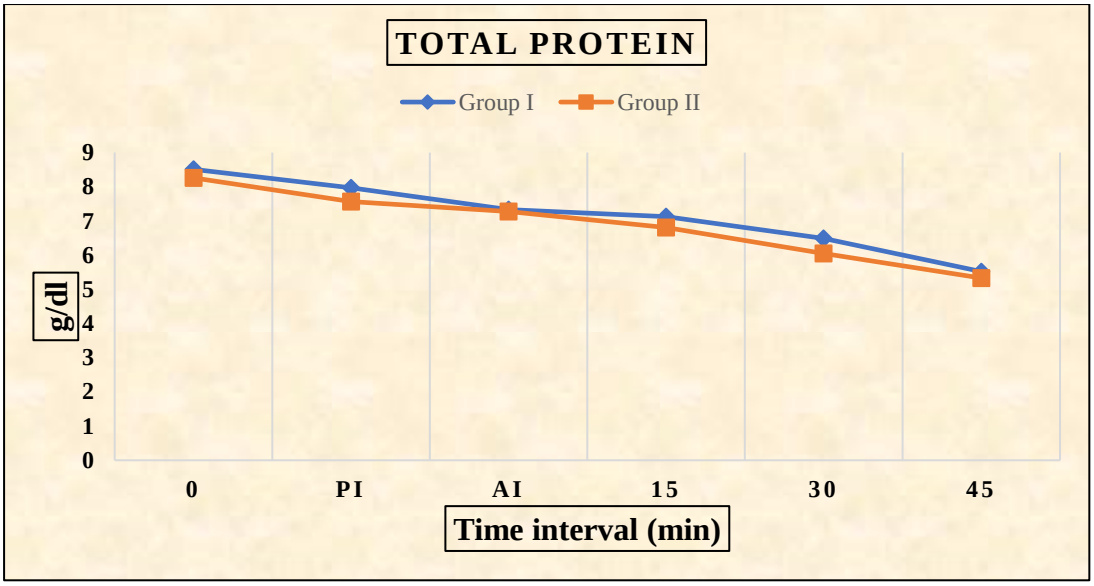

Chart 4.17 Mean values of total protein at different time intervals

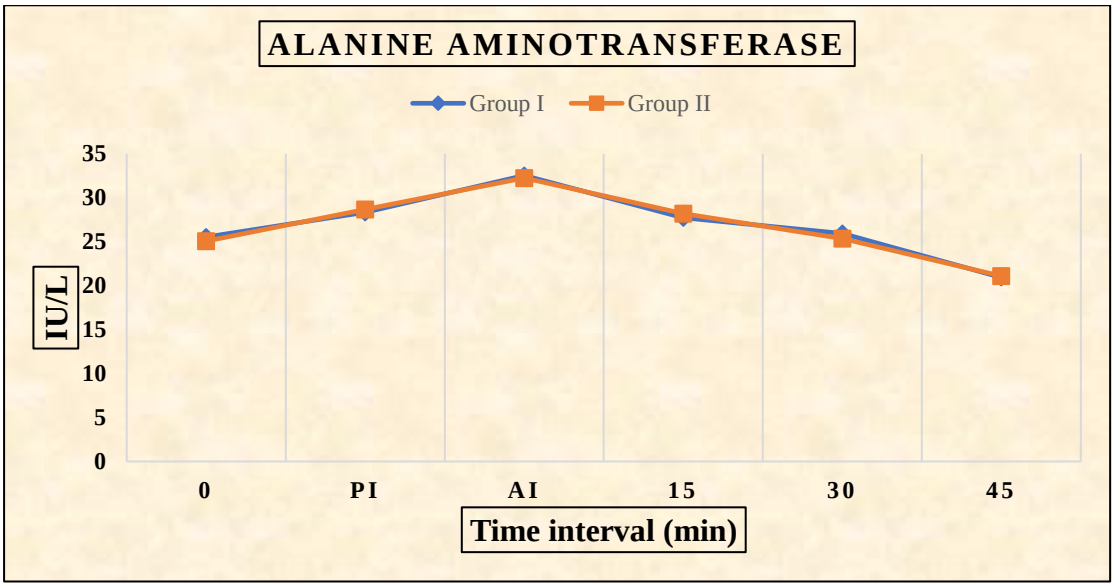

Chart 4.18 Mean values of ALT at different time intervals

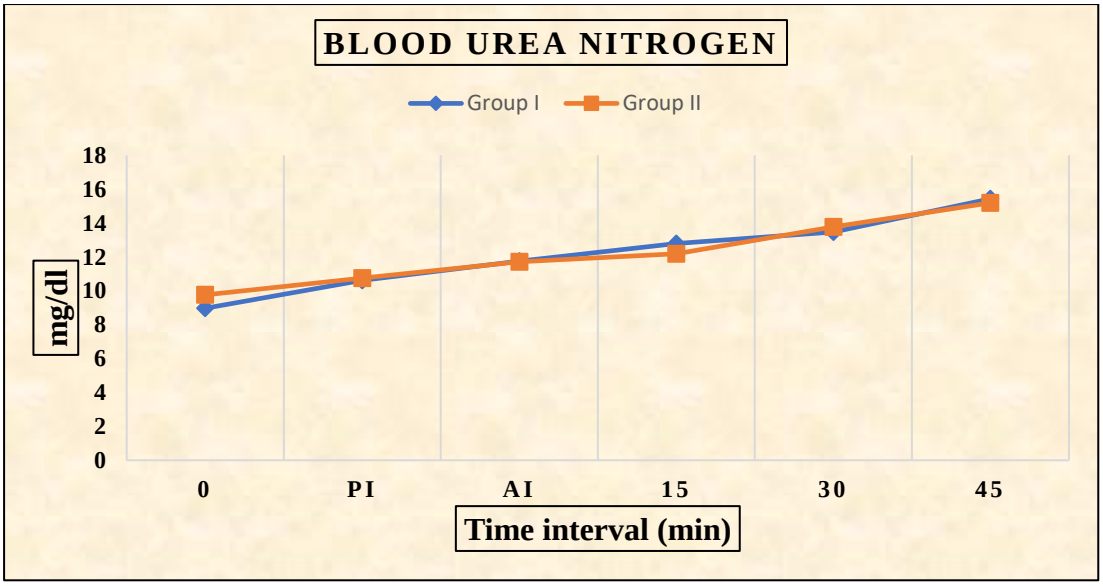

Chart 4.19 Mean values of BUN at different time intervals

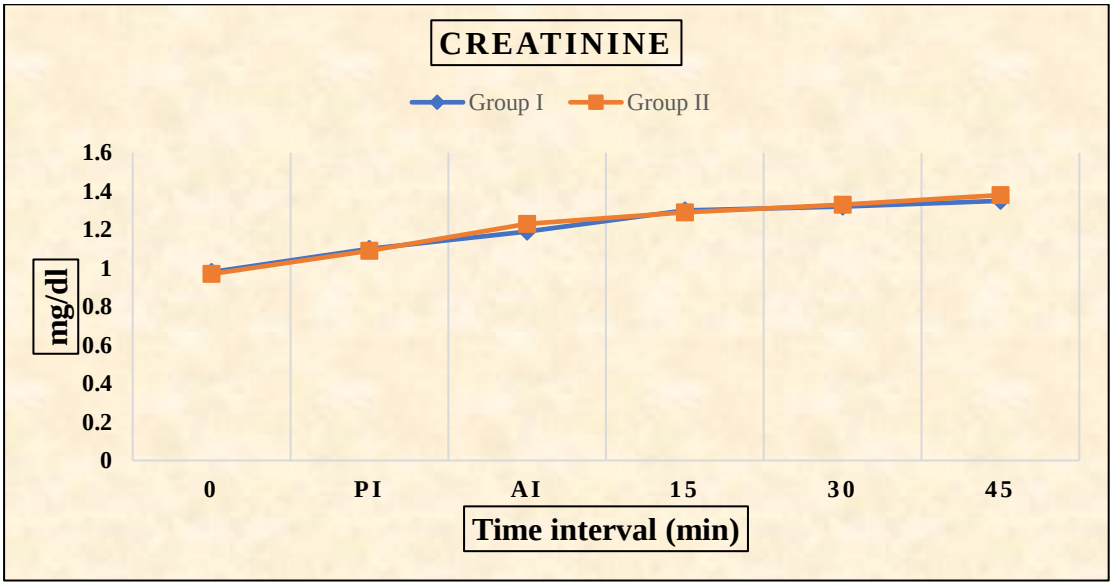

Chart 4.20 Mean values of creatinine at different time intervals

CHAPTER 5

SUMMARY AND CONCLUSIONS

The present clinical study was carried out in 12 clinical cases presented for different surgical interventions with an objectives to assess the sedative effect of xylazine and dexmedetomidine with butorphanol, to study the dose-sparing effect of butorphanol-xylazine/dexmedetomidine combination on propofol and to evaluate and compare clinico-physiological and haemato-biochemical parameters of both the anaesthetic protocols.

All the dogs were first premedicated with butorphanol @ 0.2 mg/kg BW, intramuscularly and then after 15 minutes, dexmedetomidine @ 5 μg/kg BW and xylazine @ 0.5 mg/kg BW were administered intravenously in group I and II respectively. Anaesthesia was induced by intravenous administration of 1% propofol till effect in both the groups five minutes after administration of preanaesthetic and maintained by isoflurane with 100% oxygen throughout the surgery.

The research results are summarized and following are the salient findings of the present study.

5.1 SUMMARY

The induction dose of propofol was 0.90±0.13 and 1.29±0.26 mg/kg in group I and II respectively. Dexmedetomidine and xylazine produced excellent quality of sedation with butorphanol. Smooth induction with rapid transition from conscious to anaesthetized state was observed with the propofol. The quality of maintenance anaesthesia was excellent with adequate analgesia, muscle relaxation and sufficient anaesthetic depth to perform surgery in both the groups. Recovery was smooth and uneventful without any complication.

All clinico-physiological parameters were within normal limits and no significant difference was observed between the groups. Rectal temperature decreases gradually and significantly after induction of anaesthesia in group I and before induction in group II. Respiration rate decreased gradually and significantly after premedication which remained low compared to base values up to the end of observation period in both the groups however; SpO_2 values remained non-significant throughout the study period in both the groups. Pulse rate was reduced significantly after preanaesthetic administration which gradually and nonsignificantly returned to near base value at 50 minutes in both the groups. Non-significant difference was

observed in the mean values of systolic blood pressure in group I and significant decrease in group II after 40 minutes of induction. Diastolic blood pressure was significantly reduced after induction in group I and 30 minutes after induction in group II whereas, mean arterial blood pressure showed significant decrease after 20 minutes of induction in group I and 40 minutes of induction in group II.

Haematological study revealed gradual and significant decrease in haemoglobin after induction and thereafter at 30 and 45 minutes after induction in group I; while, non-significant decrease was observed in group II. Significant decrease was observed in PCV at 30 and 45 minutes after induction in group I; while, non-significant decrease was seen in group II. There was non-significant decrease in total erythrocyte count in both the groups. Total leukocyte count decreased non-significantly in both the groups. Neutrophils count decreased nonsignificantly up to end of observation in both groups as compared to the base values. Lymphocyte count increased nonsignificantly in both the groups whereas; monocytes increased non-significantly before and after induction and thereafter, it decreases non-significantly at 15, 30 and 45 minutes after induction in both the groups. Nonsignificant increase in eosinophil count was observed after induction and non-significant decrease before induction and thereafter at 15, 30 and 45 minutes after induction in both the groups. Eosinophil count showed slight increase after induction which decrease after 30 minutes than the base values in both the groups. Blood glucose level increased significantly at 15, 30 and 45 minutes after induction of anaesthesia in both the group.

Plasma biochemical parameters revealed no significant difference between the groups. Gradual and significant decrease in mean values of total protein was observed after induction and at 15, 30 and 45 minutes after induction in group I and at 15, 30 and 45 minutes after induction in group II. In the present study, no significant difference in the mean values of ALT was observed within and between the groups. Blood urea nitrogen showed nonsignificant increase whereas, creatinine showed significant increase up to end of observation when compared to base value in both the groups.

5.2 CONCLUSIONS

1. Butorphanol with dexmedetomidine and xylazine provided excellent quality of sedation prior to induction of anaesthesia in all the animals of both groups.
2. Dexmedetomidine and xylazine showed potent dose sparing effect on induction dose propofol in dogs.

3. Propofol produced smooth induction without any complication.
4. Maintenance of anaesthesia was excellent with smooth recovery using isoflurane without any complication.
5. All clinico-physiological and haemato-biochemical parameters stayed within normal physiological limits in both the groups however, more significant changes were observed in dexmedetomidine-propofol combination than xylazine-propofol combination.

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