STUDIES ON THE EFFICACY OF ACEPROMAZINE AND MEDETOMIDINE AS PREMEDICANTS TO PROPOFOL ANAESTHESIA IN CANINES

A dissertation submitted to the

INDIRA GANDHI KRISHI VISHWAVIDYALAYA, RAIPUR

By

SANJAY DUBEY

IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF

MASTER OF VETERINARY SCIENCE

In

VETERINARY SURGERY AND RADIOLOGY

ROLL NO. - 2616 **2003** **ID. NO. - PG/VETY/2001/03**

DEDICATED

TO

JYOTSNA

CERTIFICATE – I

This is to certify that the thesis entitled **"Studies on the efficacy of acepromazine and medetomidine as premedicants to propofol anaesthesia in canines"** submitted in partial fulfillment of the requirement for the degree of "**Master of Veterinary Science"** of Indira Gandhi Krishi Vishwavidyalaya, Raipur (C.G.), is a record of bonafied research work carried out by **Sanjay Dubey**, under my guidance and supervision. The subject of the thesis has been approved by the student's Advisory Committee and the Director of Instructions.

No part of the thesis has been submitted for any other degree or diploma or has been published/ published part has been fully acknowledged. All assistance and help received during the course of investigations has been duly acknowledged by him.

Dated: 16/01/04

(S.K.Tiwari)
Chairman, Advisory Committee

THESIS APPROVED BY STUDENT'S ADVISORY COMMITTEE

Chairman : Dr. S.K. Tiwari, Professor and Head.

Member : Dr. Raju Sharda, Associate Professor.

Member : Dr. Sushovan Roy, Professor and Head.

Member : Dr. R.P. Tiwari, Professor and Head.

Member : Dr. Mohan Singh, Professor and Head. 15.1.04

Member : Dr. O.P.Mishra, Professor. 15-1-04

CERTIFICATE – II

This is to certify that the thesis entitled **"Studies on the efficacy of acepromazine and medetomidine as premedicants to propofol anaesthesia in canines"** submitted by **Sanjay Dubey**, to the **Indira Gandhi Krishi Vishwavidyalaya, Raipur (C.G.)**, in partial fulfillment of the requirement for the degree of "**Master of Veterinary Science**" in the Department of Veterinary Surgery and Radiology, College of Veterinary Science and animal Husbandry, Anjora, Durg, has been approved by the student's advisory committee after oral examination in collaboration with the external examiner.

23/2/04

EXTERNAL EXAMINER

23/02/04

MAJOR ADVISOR

23/02/04

HEAD OF DEPARTMENT

10/3/04

DIRECTOR OF INSTRUCTIONS

DATED 23/02/04

ACKNOWLEDGEMENT

At the outset I take this opportunity to express my profound sense of gratitude to **Dr. S.K. Tiwari,** Professor and Head, Department of Surgery and Radiology, College of Veterinary Science and Animal Husbandry, Anjora, Durg (Chhattisgarh), the chairman of advisory committee for his expert, meticulous probity, tremendous contemplation, magnificent ecstasy, marvelous guidance, constructive criticism and pains taking help provided by him during the present investigation and preparation of the manuscript. By working under the authority like him, I have inculcated confidence and innovative thinking which will have a lasting influence in my career.

I am grateful to **Dr. Raju Sharda**, Associate Professor, Department of Veterinary Surgery and Radiology for his generous support and help.

Heartily, I express my sincere obligation and earnest thanks to **Dr. Sudhakar Jogi**, Dean, College of Veterinary Science and A.H. and to my advisory committee members, **Dr. S. Roy**, Professor and Head, Department of Clinical Medicine and Epidemiology; **Dr. R.P. Tiwari**, Professor and Head, Department of Veterinary Gynecology and Obstetrics and **Dr. O.P. Mishra**, Professor, Department of Physiology for their generous support, incessant motivation and valuable suggestions and all possible help rendered by them for conducting my research work.

I am obliged to **Dr. Mohan Singh**, Professor and Head, Department of Animal Breeding and Genetics for taking responsibility of statistical analysis of experimental data.

I appreciate the valuable co-operation of **M/S Bharat Serums and Vaccines Ltd**. Thane for ample supply of propovan that made possible to complete the work in scheduled time.

I am extremely indebted to **State Veterinary and Animal Husbandry Department** of Chhattisgarh for providing me the opportunity as a departmental candidate.

I wish to express my sincere thanks to **Late Dr. K.D. Pamnani, Dr. Y.C. Saxena**, Deputy Director Veterinary Services and **Dr. N.K. James**, Joint Director Veterinary Services for their generous support and help rendered during my study and research work.

I am also thankful to my seniors **Dr. D.S. Shinkar**, **Dr. M.S. Chonde**, **Dr. R.B. Ghatge**, **Dr. D.D. Dubey**, **Dr. C.N. Galdhar**, **Dr. Shabbir Ahmed** for their incessant help and co-operation at each stage of the study.

My sincere and profound thanks to **Dr. P. Suryavanshi**, **Dr. K.M. Kumar**, **Dr. Shivamani**, **Dr. R. Sharma**, **Dr. N. Sharma** and **Dr. Faiyaz Ahmed** for rendering me timely help and encouragement.

I can not forget help and assistance rendered by **Shri Gajendra Patle**, **Manbahal Rajput** and **Rajkumar Rajput** during my research work.

Ever-willing co-operation extended by the academic staff, other college staff and library staff in particular is highly acknowledged.

Words can not express my deep feelings to offer my profound sense of gratitude and reverence to my beloved parents **Shri Ram Harsh Dubey – Smt. Neelam Dubey** and parents-in-law **Prof. Jugal Kishore Pandey – Smt. Tarini Pandey** for their blessings and devotion.

I thank my closest friends **Dr. Sudhir Yadav**, **Dr. Rajeev Deoras**, **Dr. Rajesh Pandey**, **Dr. Sanjay Jain**, **Dr. Deepak Chandrakar** and **Mr. Shree Kant Tiwari** for their constant encouragement and good-wishes.

I shall fail in my duty if don't express my heartfelt regards to my lovely daughters **Shivali and Sakshi**. Although they suffered most during my research work but their co-operative and affectionate approach generated an extra zeal in my heart for my work. I want to express similar feelings for my wife **Jyotsna**, her devotion and support could not be expressed in words.

At last, I want to reserve a special word of thanks for all those who helped me during my research work.

Date: 15.01.2004.

Place: Anjora, Durg.

Sanjay Dubey

Table of Contents

List of Tables

List of Figures

List of Abbreviations

@	- At the rate of
^{0}F	- Degree Fahrenheit
µg/kg	- Microgram per kilogram
ALT	- Alanine amino transferase
APTT	- Activated partial thromboplastin time
AST	- Aspartate amino transferase
B.Wt.	- Body weight
BUN	- Blood urea nitrogen
cm	- Centimeter
CNS	- Central nervous system
ECG	- Electrocardiogram
EEG	- Electro encephalogram
et al.	- et alia (and other)
$EtCo_2$	- End tidal carbon-dioxide
Fig.	- Figure
g/L	- Gram per liter
Hb	- Haemoglobin
Hrs.	- Hours
i.e.	- id est (that is)
I/M	- Intramuscular
I/V	- Intravenous
Kg	- Kilogram
MAP	- Mean arterial pressure
MCH	- Mean corpuscular haemoglobin
MCHC	- Mean corpuscular haemoglobin concentration
MCV	- Mean corpuscular volume
MEq./L	- Milli equivalent per liter

Introduction

CHAPTER – I INTRODUCTION

Anaesthesia is a state of unconsciousness characterized by analgesia (pain relief), amnesia (loss of memory) and muscle relaxation. Premedicants are used to allay anxiety, calm down the patient and elicit an anaesthetic adjuvant effect.

Anaesthetic agents given parenterally are generally depressants affecting the entire central nervous system, cardiovascular system, respiratory system and to lesser extent the liver and kidney function. No anaesthetic posses all the qualities of an ideal anaesthetic, therefore balanced anaesthesia is achieved by combining two or more drugs to achieve adequate sedation, analgesia and muscle relaxation.

Propofol, a lipophilic alkylphenol (2,6,di isopropylphenol), is a new short acting, rapidly metabolized intravenous anaesthetic agent. Anaesthesia produced by propofol is characterized by rapid onset, short duration, lack of cumulation on repeated administration and lack of excitatory effect during induction, maintenance or recovery (Bufalari *et al.,* 1996). It causes rapid loss of consciousness in 20 to 40 sec. following intravenous administration. It metabolizes ten times faster than thiopentone sodium (Duke, 1995). Duration of anaesthesia is ten minutes and complete recovery occurs in 25 to 30 min. The muscle relaxation is excellent and degree of analgesia is suitable for minor surgical procedures (Genevois *et al.*, 1988). Premedication with

medetomidine and acepromazine reduces the dose of propofol required for anaesthesia and also increases the duration of anaesthesia (Bufalari *et al.*, 1995). After awakening from anaesthesia, the patient does not show hangover effect and is bright and alert. Propofol can be used as a safe anaesthestic in dogs suffering with blood coagulation disorders (Berbish *et al.*, 1998).

Medetomidine ([1-(2,3-dimethylphenyl) ethyl]-1H-imidazole), it is a thiazine derivative and is an α_2-agonist which acts at α_2-adrenoceptors situated in the central and peripheral nervous system on pre and postsynaptic neurons. The presynaptic α_2-adrenoceptor action is of inhibition, where it has a negative feedback on the presynaptic neuron inhibiting release of its neurotransmitter. The CNS depression results in sedation, emesis and mild to moderate analgesia. Intravenous administration of medetomidine results in rapid sedation and the effect of higher doses are deeper and of longer duration (Kramer *et al.*, 1996). The combination of medetomidine with propofol provides better quality anaesthesia (Hellebrekers and Sap, 1997). Higher dose of medetomidine requires less propofol for induction and infusion and allows maintenance of more stable anaesthesia (Hammond and England, 1994). The action of medetomidine can be reversed rapidly with atipamezole and thus greatly expands the safety and utility of the drug (Cullen, 1996)

Acepromazine, a phenothiazine compound is one of the most commonly used tranquilizers in veterinary surgery, which acts on the

CNS by depressing the brain stem and connections to the cerebral cortex (Robin, 1987). It produces general calming and reduction in motor activity besides an anti-emetic effect. Its action is quick by intravenous route and prompt by subcutaneous route. It is used mostly as a pre-operative medication and occasionally for car-sickness by oral route.

Reports regarding combination of propofol with medetomidine and acepromazine for performing surgery in clinical cases are limited. Therefore, the present research was designed to evaluate the suitability of medetomidine and acepromazine as premedicants to propofol anaesthesia in canines with the following objectives:-

1) To investigate the clinical effects of Atropine sulphate-Propofol, Atropine sulphate-Acepromazine-Propofol and Atropine sulphate-Medetomidine-Propofol in dogs.
2) To assess the physiological and cardiopulmonary alterations in response to these combinations.
3) To evaluate the changes in haematological and biochemical profiles in response to these combinations.
4) To study and compare the degree of analgesia and muscle relaxation produced by these combinations.
5) To judge the suitability of these combinations in short and long duration surgical interventions in canine surgical patients.

Review of literature

2.1 Atropine sulphate:

Atropine is an alkaloid extracted from the leaves of the plant atropa belladonna. Preanaesthetic use of atropine prevents salivary secretion and inhibits the bradycardiac effects of vagal stimulation. Chemically, atropine consists of an aromatic tropic acid moiety combined by an ester linkage to an organic base, tropine.

Atropine is a competitive inhibitor of acetylcholine at the muscarinic receptors of the effector cells like smooth muscle, cardiac muscle and glandular tissues. The actions of atropine on all the cholinergic receptors are not equal. Salivary and cholinergic sweat glands are highly susceptible to atropine where as gastrointestinal and urinary tract smooth muscles are less sensitive and larger doses are needed for vagolytic effects on heart.

Kirk (1990) quoted the adverse effects of anticholinergic drugs in small animals, which are dose related. As the dose was increased there was dry mouth, tachycardia, miosis and changes in CNS activities like excitement and confusion.

Roush *et al.* (1990) studied the effects of atropine and glycopyrrolate on oesophageal, gastric and tracheal pH in anaesthetized dogs and concluded that preanaesthetic use of atropine and

glycopyrrolate had no effect on oesophageal, gastric and tracheal pH but did result in increased heart rate.

Bore (1991) compared the effects of atropine by two different routes of administration that is endotracheal and intravenous routes and found positive relationship between dose and responses to atropine given endotracheally. The increase in heart rate following atropine administration were similar in terms of magnitude and speed of onset when given by endotracheal route @ 0.06 mg/kg as compared to that obtained by intravenous route @ 0.04 mg/kg.

Sventine and Bjegovi (1995) compared the effects of atropine, scopolamine and 3-quinuclidinyl benzylate (QNB) on spontaneous and stimulated cortical acetylcholine (Ach) release in 21 anaesthetized cats. Atropine (5.0 mg/kg I/V) had minimal effect on spontaneous acetylcholine release.

Rishniw *et al.* (1996) studied the characterization of chronotropic and dysarrythmogenic effects of atropine in dogs and vagally mediated bradycardia was induced with morphine and fentanyl citrate in seven healthy dogs. Atropine was administered I/V, I/M, and S/C @ 0.02 mg/kg body weight. All the dogs developed second degree atrioventricular (AV) block after I/V administration of atropine and 71% dogs developed AV block after S/C or I/M administration. The AV block arose and resolved more rapidly with I/V administration than with S/C or I/M administration. The AV block was principally attributable to an increase

in the ventricular rate. Atropine potentiated base line ventricular bradycardia in 62% of the experimental animals. Duration of bradycardia potentiation was longer with S/C administration (9 minutes, S/C; 1.4 minutes, I/V; 4.6 minutes, I/M). Parasympatholytic rate was higher for I/V than S/C or I/M administration (128 beats/minutes Vs 92 beats/minutes and 101 beats/minutes). It was concluded that vagally mediated bradycardia was best abolished by I/V administration of atropine.

Alibhai *et al.* (1996) investigated the effects of combination of medetomidine (40 µg/kg) and atropine (30 µg/kg) on the cardiopulmonary effects in dogs and concluded that although, atropine counteracts medetomidine induced bradycardia, its use results in prolonged and severe hypertension in association with the tachycardia.

2.2 Acepromazine and its combination with other anaesthetic drugs:

Acepromazine, the 2-acetyl derivative of promazine; a phenothiazine compound is one of the most commonly used tranquilizers in veterinary medicine, which acts on the CNS by depressing the brain stem and connections to the cerebral cortex (Robin, 1987). It produces general calming and reduction in motor activity besides an anti-emetic effect.

Pugh *et al.* (1964) reported acepromazine as a highly potent and effective sedative in canines. They used acepromazine as a

preanaesthetic sedative prior to thiopental sodium anaesthesia and reported the reduction of 48.3% dose of thiopental.

Popovic *et al.* (1972) studied the effect of acepromazine and recorded decrease in arterial blood pressure, intermittent bradycardia and decrease in respiratory rate in dogs.

Turner *et al.* (1974) observed tachycardia in dogs, five minutes after administration of acepromazine. Further, they attributed the greater popularity of acepromazine to its higher potency, fewer side effects and rapid onset of action.

Alexander (1976) compared the effect of acepromazine and chlorpromazine and reported that the acepromazine was more potent and less erratic in its ataractic activity than chlorpromazine.

Booth (1982) stated that acepromazine was more potent than chlorpromazine and found its higher effectiveness parenterally even in small doses. However, it was reported to cause intermittent bradycardia, sinoatrial arrest, hypotension and marked decrease in respiratory frequency in dogs.

Short *et al.* (1982) administered acepromazine @ 0.5-mg/0.45 kg body weight in canines and studied the reversal of acepromazine sedation with doxapram. They reported persistence of immobilization of dogs for two hours.

Waechter (1982) found unusual reactions with acepromazine in dogs where one dog turned vicious, snarled while other started biting. He

stated no pharmacologic or physiologic reason for this phenomenon, but it was thought as an idiosyncrasy.

Hatch *et al.* (1983) administered acepromazine in dogs (0.1 mg/kg) and reported that the dose of pentobarbital required for anaesthesia was reduced by forty-seven percent.

Baggot *et al.* (1984) observed a delayed time of recovery from anaesthesia in dogs premedicated with acepromazine while Farver *et al.* (1986) observed decrease in respiratory rate in dogs following the administration of 0.2 mg/kg of acepromazine.

Heard *et al.* (1986) administered acepromazine with halothane in dogs. They noted reduction in requirement of halothane upto 40% when acepromazine was administered @ 4 mg/kg body weight.

Watkins *et al.* (1987) used acepromazine @ 0.02 to 0.04 mg/kg as a preanaesthetic to propofol anaesthesia in dogs and observed 30% and 50% reduction in induction and maintenance dose of propofol respectively.

Webb and O'Brien (1988) observed reduction in anaesthetic requirement of both halothane and isoflurane in dogs premedicated with acepromazine @ 0.2 mg/kg body weight.

Morgan and Legge (1989) studied induction of propofol anaesthesia in unpremedicated and premedicated dogs and reported reduction of propofol dose from 6.55 mg/kg to 4.5 mg/kg in acepromazine premedicated dogs.

Feini *et al.* (1990) induced and maintained anaesthesia with propofol by its continuous infusion by electrically operated syringe for a period of one hour, following premedication with atropine and acepromazine. They concluded that it was an excellent method of anaesthesia than inhalation anaesthesia.

Weaver and Raptopoulos (1990) stated the mean induction dose of propofol was 5.2 ± 2.3 mg/kg in unpremedicated dogs and 3.6 ± 1.4 mg/kg in acepromazine premedicated dogs. They reported faster and complete recovery in 16.4 ± 9 minutes in unpremedicated dogs and comparatively longer recovery (40.4 ± 26.7 minutes) in premedicated dogs. Further, they concluded that premedication did not affect recovery times and the incidence of side effects was very low.

Geel (1991) found reduction in induction dose of propofol from 6.9 ± 0.9 mg/kg in unpremedicated dogs to 4.3 ± 1.4 mg/kg in acepromazine medicated dogs.

Jones (1992) suggested the use of acepromazine in dogs for a calm and quiet sedation. He further advised its use to reduce the amount of general anaesthetic as well as for a quiet recovery.

Light *et al.* (1993) reported that the acepromazine was found more effective for reducing the pain and anxiety behavior of dogs.

Smith *et al.* (1993) stated that in dogs the effect of acepromazine lasts for 4 to 6 hours and its recovery is free from excitement.

Stephien *et al.* (1995) observed depression of cardiac function, respiratory rate and mean systemic arterial pressure without any change in heart rate following acepromazine injection.

Nazneen (1998) studied the sedative effect of acepromazine in canines and concluded that acepromazine had minimal adverse effect on cardiorespiratory system.

Fantoni *et al.* (1999) reported that acepromazine had no significant effect on respiratory rate. However, it had sigfnificant effect on diastolic and systolic blood pressure.

Hall *et al.* (1999) stated that there was statistically significant reduction in the dose of propofol for anaesthetic induction in cats when they were premedicated with morphine (0.2 mg/kg body weight I/M) or acepromazine (0.2 mg/kg body weight I/M).

Rezende *et al.* (2002) concluded that acepromazine minimizes ventricular epinephrine-induced arrhythmia in dogs anaesthetized with halothane.

Thibaut *et al.* (2002) compared the anaesthetic effects of propofol as a single dose, premedicated with atropine-acepromazine and atropine-xylazine and reported that these combinations induce an adequate surgical anaesthesia in dogs without significant physiological changes.

2.3 Medetomidine and its combination with other anaesthetic drugs:

Medetomidine, 4-[1-(2,3-dimethylphenyl)ethyl]-1H-imidazole, is a very potent, efficacious and selective agonist of α_2–adrenoceptors in central and peripheral nervous system. (Savola *et al.*, 1986). Medetomidine induces sedation and analgesia in laboratory animals. After high doses, hypnotic or even anaesthetic properties are seen (Salova *et al.*, 1986). The α_2/ α_1 selectivity of medetomidine is 1620 as compared to 260, 220 and 160 for detomidine, clonidine and xylazine, respectively (Virtanen, 1989).

Medetomidine induces a dose-dependent decrease in the release and turnover of noradrenaline, dopamine and serotonin in the CNS as measured by changes in metabolite concentrations or using pharmacological intervention technique. Inhibition of sympathetic tone in the CNS by medetomidine leads to a characteristic pattern of pharmacodynamic responses including hypotension, bradycardia, sedation, relief of anxiety, analgesia and hyperthermia. At high doses, medetomidine has hypnotic or anaesthetic effects, a property which distinguishes it clearly from detomidine, clonidine, and other α_2 agonists.(Virtanen *et al.*, 1988)

Lombard *et al.* (1988) used medetomidine @ 30 µg/kg I/M as a sedative drug for teeth cleaning in dogs and observed that the drug

caused a considerable reduction of the body temperature and heart rate over 6 hrs period of monitoring. The respiratory rates increased over first 30 min and later decreased below control values in all the dogs. Systolic arterial pressure did not change significantly. On electrocardiogram, sinus bradycardia, marked sinus arrhythmia with sinus pauses, first and second degree AV-blocks, supraventricular premature contractions and paroxysmal tachycardia. All measured parameters returned to normal values at 24 hrs after sedation.

Nilsfors *et al.* (1989) used medetomidine as a sedative and analgesic agent to two hundred eighty three dogs with the mean dose varying from 17 µg/kg I/M for X-ray examination to 31 µg/kg I/M for clinical examinations. An adequate analgesic effect was demonstrated at higher dose with potent bradycardia with in 15 min post administration. No influence of breed, sex or age was found. Vomiting was observed in 8% of the cases.

Vaha Vaha (1989) studied the clinical efficacy of medetomidine and reported that it produced a reliable state of sedation, relaxation and recumbency suitable for small animal practice. In dogs, the optimum clinical dose for examination, clinical procedures and minor surgical interventions seems to be 30 to 40 µg/kg I/M. Other effects of medetomidine reported were bradycardia, nausea, vomiting and occasional muscle jerking.

Manners (1990) suggested that if higher dose rate of medetomidine is used, lower dose of anaesthetics is recommended. Full onset of sedation with medetomidine (15 to 20 min. after I/M injection) should be allowed to develop before anaesthesia is induced to prevent overdosing.

Vainio (1991) evaluated the anaesthetic effects of medetomidine-propofol combination in Beagles and concluded that it was a promising anaesthetic regimen. Oxygen enriched inspired air should be used for its clinical use.

Culen and Reynoldson (1993) compared the duration of anaesthetic and cardiopulmonary effects of propofol (6.55 mg/kg I/V), xylazine (0.8 mg/kg I/M), medetomidine (30 μg/kg I/M), xylazine plus propofol (3 mg/kg I/V) and medetomidine plus propofol (3 mg/kg I/V) in dogs and reported that both premedicants prolonged the propofol anaesthesia accompanied by apnoea and hypoxaemia but with medetomidine the hypoxaemia was most evident and hypertension was constantly recorded.

Hammond and England (1994) mentioned that higher dose of medetomidine required less propofol for induction and infusion and allowed a more stable anaesthesia to be maintained. The respiratory rate was reduced in the dogs given 5 or 10 μg/kg medetomidine, unchanged in dogs given 20 μg/kg and increased in dogs given 40 μg/kg medetomidine.

Bufalari *et al.* (1995) stated that both acepromazine and medetomidine as preanaesthetic to propofol anaesthesia reduced the dose of propofol required for induction of anaesthesia. Medetomidine significantly reduced the dose of propofol required for the maintenance of anaesthesia for 30 min. Medetomidine/propofol group had a significantly higher blood pressure and longer duration of anaesthesia and recovery.

Alibhai *et al.* (1996) reported that administration of medetomidine alone caused severe bradycardia, which was followed 15 min. later by tachycardia and hypertension.

Bufalari *et al.* (1996) observed that anaesthetic duration was shorter with propofol alone and prolonged with medetomidine as preanaesthetic which was reversible with atipamezole.

Cullen (1996) reported that medetomidine is a potent alpha $_2$ adrenoceptor agonist and stimulates receptors centrally to produce sedation and analgesia and receptars centrally and peripherally to cause bradycardia and decreased cardiac output. The drug frequently caused hypotension, hypoxemia, reduced gastrointestinal motility, hypothermia, changes to endocrine functions and occasionally vomiting and muscle twitching.

Kremer *et al.* (1996) treated different dogs with medetomidine (40 µg/kg or 80 µg/kg) or xylazine (1.0 mg/kg) by I/M or I/V routes and concluded that the onset, depth and duration were affected by the dose and route of administration. In the medetomidine treated dogs, I/V

administration resulted in more rapid sedation and the effects of the higher dose were deeper and longer lasting. Treatment with specific α_2 antagonist atipamezole reversed the sedation and cardiovascular and pulmonary effects due to medetomidine with in minutes.

Rand *et al.* (1996) reported that echocardiographic effects of medetomidine and xylazine were similar. Because of their cardiac depressent effects both the drugs should be used with care in sick dogs.

Hallebrekers and Sap (1997) suggested that medetomidine is a satisfactory sedative-analgesic premedicant and its combination with propofol provides better quality anaesthesia.

Hall *et al.* (1997) stated that there were significant difference in the systemic clearance and mean resident time (MRT, I/V) when propofol was given alone as compared with medetomidine premedication in dogs.

Hellebrekers *et al.* (1998) used combination of medetomidine either with propofol or ketamine and reported that the quality of anaesthesia was considered to be smooth in 89 percent of the propofol group but in only 63 percent of the ketamine group.

Scabell *et al.* (1999) concluded that the 4 anaesthetic combinations i.e. medetomidine (40 µg/kg I/V) in combination with diazepam (0.4 mg/kg), ketamine (1 mg/kg), levomethadone (0.3 mg/kg) or propofol (2 mg/kg) provide similar levels of anaesthesia and are suitable for use in healthy dogs.

Komar and Balicki (2000) reported that premedication with atropine and medetomidine to propofol anaesthesia caused increase in heart rate, arterial pressure and vascular resistance and decrease in cardiac output. After application of atipamezole, the cardiac output was elevated, however, the arterial pressure and vascular resistance decreased for 5 min. and increased later on.

Grimm *et al.* (2001) evaluated the anaesthetic and cardiorespiratory effects of medetomidine (22 μg/kg I/M) with intravenous butorphanol (0.22 mg/kg) and intravenous atropine (0.22 mg/kg) followed by intravenous propofol (2.2 mg/kg) and reported mild acidaemia, hypercapnia, hypoxaemia, decreased SaO_2 and PaO_2 after propofol administration.

Ozaydin *et al.* (2001) reported that the combination of medetomidine (10 μg/kg I/M) as preanaesthetic to propofol (3.5 mg/kg I/V) and ketamin (10 mg/kg I/V) induced sedation in 2 min., anaesthesia for 8 min. and complete recovery between 68 to 100 min. (mean 86.1 min.). Decrease in rectal temperature and bradycardia were noted throughout the anaesthesia. Similarly, decrease in respiratory rate in all the animals and temporary apnoea was recorded in some of the animals. Non significant alterations were obtained in hematocrit, haemoglobin, erythrocyte and leukocyte counts during the anaesthesia.

Rauser and Lexmaulova (2002) compared the effect of medetomidine (10 μg/kg) with butorphanol (0.1 mg/kg) and

medetomidine (10 μg/kg) with bupernorphine (0.01 mg/kg) used as intravenous premedication and reported to induce good sedation within 5 min. The anaesthesia was induced by intravenous administration of propofol and maintained by a mixture of O_2/N_2O/halothane. There was no difference in the dose of propofol for induction of anaesthesia. However, the number of readministration and the total dose of propofol readministered, were significantly lower when premedicating by medetomidine-bupernorphine.

2.4 Propofol and its combination with other anaesthetic drugs :

Propofol, 2-6 diisopropyl phenol is a short intravenous anaesthetic agent suitable for induction and maintenance of general anaesthesia. Propofol is less soluble in aqueous solution (Glen *et al.*, 1985) and hence is formulated in white oil in white emulsion. The present isotonic formulation contains active ingradient propofol (10 mg/ml), soyabean oil (100 mg/ml), Glyserol (22.5 mg/ml), egg lecithin (12 mg/ml) and disodium acetate (0.005%) with sodium hydroxide to adjust pH (7 to 8.5).

Glen *et al.* (1985) found that propofol has no anticonvulsant effect in animals in contrast to thiopentone. No potentiation of propofol anaesthesia was found following pretreatment with diazepam or alcohol. Acute administration of beta-receptor antagonist was tolerated during anaesthesia with propofol. Propofol was found to have no effect on ADP

induced platelet aggregation, whole blood clotting time, bronchomotor tone and gastrointestinal motility.

Hall and Chamber (1987) observed that in canines the continuous infusion of propofol to maintain anaesthesia in healthy dogs was safe but less satisfactory than the use of halothane or nitrous oxide.

Watkins *et al.* (1987) reported that induction of propofol anaesthesia was smooth and it was possible to anaesthetize the animal by intermittent injections. Premedication with acepromazine reduced the mean induction dose by 30 percent and the maintenances dose by more than 50 percent.

Brearely *et al.* (1988) reported that decrease in heart rate after induction of propofol anaesthesia was due to decreased sympathetic stimulation in excited animals and not because of cardiac depression.

Claeys *et al.* (1988) observed decrease in arterial blood pressure following intravenous injection of propofol and stated that propofol depresses the sympathetic neural outflow resulting in decreased sympathetic vascular resistance.

Genevois *et al.* (1988) reported that single intravenous injection without any premedication gave a very brief period of anaesthesia with slight respiratory depression. Analgesia and muscle relaxation was sufficient for painful radiography, opening of an abscess and reduction of luxation.

Langely and Heel (1988) noted rapid distribution of propofol in the body without any cumulative effect and thus it allowed quick recovery.

Goodchild and Serrao (1989) concluded that anaesthesia with propofol might be accompanied by decreased cardiac output secondary to reduction in preload by a direct vasodilatory effect in dogs. It was hypothesized that cardiac output and arterial pressure preserve well at normal anaesthetic blood concentration of propofol if the preload is maintained.

Morgan and Legge (1989) studied the clinical efficacy of propofol in dogs and cats and reported that premedication with tranquilizers like acepromazine, diazepam and xylazine reduced the mean induction doses of propofol.

Weaver and Roptopuluas (1990) used propofol in dogs and cats either unpremedicated or premedicated with acepromazine, papavertum, diazepam, pethidine, atropine and scopolamine in different combinations. The mean (± SD) induction doses of propofol in unpremedicated and premedicated animals were 5.2 ± 2.8 mg/kg and 3.6 ± 1.4 mg/kg, respectively for dogs and 5.0 ± 2.8 mg/kg and 5.3 ± 4.3 mg/kg for cats.

Fonda (1991) used propofol in dogs premedicated with atropine (0.03 mg/kg) and acetylepromazine (0.05 mg/kg) intramuscularly followed 20 minutes later by intravenous injection of propofol (3 mg/kg) as an induction dose. Propofol was given @ 0.3 mg/kg/min. as a

maintenance dose immediately. Continuous infusion anaesthesia under different noxious stimuli provided similar recovery times. Higher infusion doses of propofol were necessary for endoscopic examination and for younger animals, whereas lower infusion doses were sufficient for repeated anaesthesia, radiotherapy and for elderly animals.

Geel *et al.* (1991) studied the effect of premedication on the induction and maintenance of propofol anaesthesia in dogs and cats and found that when opoid or medetomidine were used as premedicant, the induction dose of propofol decreased substantially by 25 percent to 75 percent, but these preanaesthetic agents might cause significant respiratory depression manageable only by 100 percent oxygen therapy and mechanical ventilation.

David (1992) evaluated the anaesthetic efficacy of propofol in unpremedicated dogs and reported significant decrease in respiratory rate and central venous pressure. He also found longer duration of surgical anaesthesia and recovery time in premedicated dogs.

Nakamura *et al.* (1992) measured the direct effect of propofol on isolated canine cerebral, coronary, mesenteric, femoral and renal arteries and demonstrated that clinically relevant concentration of propofol did not have direct vasodilatory effect.

Watney and Pablo (1992) determined the median effective dosage (ED50) of propofol for induction of anaesthesia in dogs premedicated with acepromazine @ 0.05 mg/kg body weight and in unpremedicated

dogs. The ED 50 was 2.2 mg/kg in premedicated dogs and 3.8 mg/kg in unpremedicated dogs. The mean total dose of propofol required to induce anaesthesia in premedicated dogs was 2.8 ± 0.5 mg/kg and 4.7 ± 1.3 mg/kg in unpremedicated dogs. Signs of excitement were observed in five of the unpremedicated dogs but in none of those that were premedicated.

Waterman and Hashim (1992) studied the effect of thiopentone and propofol on oesophageal pressure in bitches. The bitches were premedicated with acepromazine and atropine. Oesophageal sphincter pressure (OSP) and gastric pressure were significantly lower in the animals anaesthetized with propofol as compared to those anaesthetized with thiopentone.

Combrission *et al.* (1993) reported that propofol was good drug for investigation of the urethral pressure profile in dogs.

Davies (1993) observed the excitatory phenomenon after induction of anaesthesia using propofol in dogs presented for surgery under general anaesthesia and some times maintained with propofol. Excitatory signs included muscle twitching, opisthotonus and limb hyper-relaxation, panting associated with brachiocephalicus muscle activity and tongue retraction.

Funkquist *et al.* (1993) evaluated anaesthesia induced with propofol (6.5 mg/kg body weight) and maintained by inhalation of isoflurane (in oxygen and nitrous oxide) in bitches undergoing caesarean section and compared the results with those of caesarean section under

epidural or general anaesthesia induced with thiopentone. The survival rate of puppies was higher after general anaesthesia induced with propofol compared with thiopentone.

Holzchun *et al.* (1993) studied the cardiopulmonary effects of propofol in hypovolaemic dogs and reported increase in oxygen utilization ratio and decrease in mean arterial blood pressure, pulmonary capillary wedge pressure, cardiac index, oxygen delivery mixed venous oxygen tension from the base line three minutes after propofol administration. Mean pulmonary arterial pressure, pulmonary vascular resistance, oxygen utilization ratio, venous mixture, arterial and mixed venous carbon dioxide tension were increased, where as mean arterial pressure, arterial oxygen tension, mixed venous oxygen content, arterial and mixed venous pH decreased from the values measured prior to propofol administration and 15 min. after propofol administration. However, by 30 min. all measurements had returned to normal.

Keegan and Greene (1993) compared the cardiovascular effects in dogs anaesthetized with continuous infusion of propofol or isoflurane. The anaesthesia induced by propofol caused higher systemic arterial pressure due to higher vascular resistance while the cardiac index was not affected. Apnea and cyanosis were observed during induction of anaesthesia with either propofol or isoflurane.

Komer *et al.* (1993) reported that continuous infusion of propofol caused a transient respiratory acidosis and decreased blood oxygenation with short lived significantly increased pulmonary shunt.

Robertson *et al.* (1993) studied the cardiopulmonary, anaesthetic and postanaesthetic effects of propofol in greyhounds and nongreyhounds and found that arterial blood pressure was well maintained in all dogs but heart rate, rectal temperature and respiratory rate were decreased during the infusion in greyhounds. In greyhounds mild respiratory acidosis was developed after 45 min. whereas in nongrehounds, arterial carbon-dioxide tension was increased at all times after propofol administration. In all the dogs, the values of PCV and total plasma proteins were unchanged during propofol anaesthesia.

Smith *et al.* (1993) found that propofol induced dose dependent adverse effects could be minimized by preanaesthetic medication. Recovery characteristics varied with preanaesthetic medication.

Vainio (1993) reported that propofol infusion after premedication with medetomidine could be a promising anaesthetic regimen but if used clinically, O_2 enriched inspiration should be used. This combination showed absence of palpebral and pedal reflexes at the surgical stage of anaesthesia.

Komer *et al.* (1993) studied the hemodynemic effects of propofol and reported that tachycardia, decreased arterial pressure and

peripheral vascular resistance, increased diastolic pressure without change in cardiac output.

Wooten and Lowrie (1993) found nonsignificant difference in cerebrospinal fluid pressure in dog anaesthetized with propofol or thiopentone.

Zoran *et al.* (1993) studied the pharmacokinetics and recovery characteristics of propofol in greyhounds and mixed breed dogs and observed significant difference in the mean concentration of propofol in blood, recovery characteristics and estimate for apparent volume distribution, volume of distribution of steady state and total body clearance. Greyhounds recovered from anaesthesia at higher concentration of propofol than did mixed breed dogs.

Hammond and England (1994) used propofol in adult beagle dogs premedicated with medetomidine. The effect of medetomidine were reversed thirty minutes after the induction with atipamezole given intramuscular at five times the original dose of medetomidine. Combination of medetomidine and propofol showed marked synergy indicated by a dose related reduction in the induction and infusion requirements for a similar degree of anaesthesia. Higher dose of medetomidine required less propofol for induction and infusion and allowed a more stable anaesthesia to be maintained. They observed that propofol did not produce any change in heart rate during infusion. Respiration rate was reduced in the dogs given 5 or 10 μg/kg

medetomidine, unchanged in the dogs given 20 μg/kg and increased in the dogs given 40 μg/kg medetomidine. Administration of atipamezole caused slower recovery in the dogs given lower dose of medetomidine and higher dose of propofol.

Bufalari *et al.* (1995) observed that premedication with acepromazine or medetomidine reduced the dose of propofol required for the induction and the maintenance of anaesthesia for 30 min. in dogs. Differences in the physiological responses between acepromazine-propofol were not significant. The dogs in the medetomidine-propofol group had a significantly higher blood pressure and a longer duration of anaesthesia and recovery.

Kramer *et al.* (1995) found the occurrence of tonoclonic convulsions in a 4-year-old Rhodesian ridge back bitch after propofol anaesthesia. In a second case propofol was used in a 3-year-old Bouvier des Flandres bitch to terminate excitement after surgery which later on turned into tonic convulsions.

Duke (1995) reported that quality of induction and recovery was good with fewer side effects in premedicated dogs and cats. Muscle relaxation was excellent and degree of analgesia was suitable for minor surgical procedures. The patient was bright and alert soon after propofol anaesthesia than after the use of thiobarbiturates.

Thurmon *et al.* (1995) reported that after premedication with medetomidine, endotracheal intubation was easy and anaesthesia was characterized by profound muscle relaxation.

England *et al.* (1996) observed that premedication with romifidine had a synergestic effect with propofol and reduced the required induction and infusion doses by more than 60% for standard level of anaesthesia with smooth recovery from anaesthesia. Propofol induced non significant alterations in heart rate, respiration rate and rectal temperature.

Gill *et al.* (1996) studied the changes in blood parameters after acepromazine premedication in propofol anaesthetized dogs and reported normal heart and respiration rates with uneventful recovery. There was decrease in haemoglobin and red blood cell count and increase in white blood cell count after laparotomy performed under anaesthesia.

Bufalari *et al.* (1997) evaluated the cardiopulmonary, anaesthetic-analgesic effects of propofol in dogs premedicated with acepromazine, butorphenol and acepromazine-butorphenol and reported apnea and bradycardia in dogs premedicated with butorphenol, acepromazine-butorphenol. Propofol lowered the arterial blood pressure without any cardiac dysarrhythmias in all the three groups. The anaesthetic duration and recovery time were longer in dogs premedicated with acepromazine-butorphenol.

Cullen and Reynoldson (1997) investigated the cardiovascular and pulmonary effects of tiletamine/zolazepam, propofol and

tiletamine/zolazepam propofol and reported increase in the mean arterial blood pressure and heart rate after tiletamine/zolazepam alone and after tiletamine/zolazepam-propofol, although propofol alone reduced MAP, caused apnea but heart rate increased transiently. The most notable change was hypoxemia in the tiletamine/zolazepam-propofol group in which the Pa CO_2 was reduced. Dogs receiving tiletamine/zolazepam, tiletamine/zolazepam-propofol showed undesirable side effects.

Kelawala and Persania (1997) found excellent muscle relaxation, short duration anaesthesia, transient apnea with no change in heart rate after induction of anaesthesia with propofol. During anaesthesia eye remained open with dilated pupil, palpebral reflexes persisted however pedal reflexes were abolished and tongue remained out side the mouth cavity.

Raptopoulous and Galatos (1997) studied the gastro oesophageal reflex during anaesthesia induced with either thiopentone or propofol in dogs and found more incidence of gastro-oesophageal reflex occurring in the propofol group due to greater decrease of lower oesophageal sphincter pressure induced by propofol than thiopentone in dogs.

Rasmussen (1997) concluded that adequate anaesthesia with reliable and rapid recovery could be achieved by premedication with a combination of medetomidine (20 µg/kg) acepromazine (0.3 mg, irrespective of body weight) and atropine (0.02 mg/kg), followed by

induction and maintenance with propofol administered with an infusion pump.

Redondo *et al.* (1997) studied the clinical efficacy of acepromazine-propofol-halothane and xylazine-propofol-halothane anaesthetic procedures in sick dogs and recorded a higher heart rate and rectal temperature during anaesthesia in acepromazine group than in the xylazine group. There were non significant difference in the respiration rate and the percentage of arterial blood saturation of oxygen. They concluded that both anaesthetic procedures were safe and effective and provided smooth and stress free recovery for all types of canine surgery.

Reid and Nolan (1997) indicated the need of lower dose when propofol was used for maintenance of general anaesthesia in geriatric dogs.

Short *et al.* (1997) investigated the cardiopulmonary effects of propofol and reported that propofol caused respiratory depression at anaesthetic dosage and supplemental oxygen administration significantly improved safety and function even in cardiopulmonary compromised dogs.

Barbish *et al.* (1998) studied the effects of ketamine hydrochloride and propofol anaesthesia after premadication with atropine, diazepam and xylazine on blood coagulation in dogs. They found that the activity of prothrombine time decreased significantly for 2 hrs. after anaesthesia in both the groups. Activated partial thromboplastine time (APTT) and

platelet count were increased for 45 and 60 min. respectively after ketamine administration. Propofol anaesthesia had no effect on APTT and platelet count. No changes in fibrinogen concentration were observed in either group after administration of anaesthesia. It was concluded that propofol could be used as a safe anaesthesia in dogs with blood coagulation disorders.

Bufalari (1998 a) reported that propofol was safe and effective anaesthetic, suitable for wide range of applications in dogs when used alone or in combination with sedatives and analgesics. Bufalari *et al.* (1998 b) evaluated the cardiovascular, pulmonary and quantitative electroencephalographic parameters of propofol for halothane and isoflurane anaesthesia in dogs and did not found apnea during induction of anaesthesia. The initial propofol medicated decrease in arterial blood pressure continued during halothane or isoflurane anaesthesia without simultaneous increase in heart rate. The result suggested that propofol in combination with inhaled anaesthetics could be used effectively and safely in dogs.

Jane *et al.* (1998) evaluated cardio-respiratory and anaesthetic effects of propofol and thiopental in dogs and reported that rapid recovery from anaesthesia was a major advantage over thiopentone anaesthesia. Time to sitting and standing for dogs was quicker and the dogs were more coordinating rapidly after propofol anaesthesia than thiopentone administration. Respiratory depression could be associated

with controlled ventilation. Prevalence of cardiac arrhythmias was also similar between the two drugs.

Kennis *et al.* (1998) investigated the effect of propofol ananesthesia on intradermally injected histamine phosphate in clinically normal dogs and found that mean weal size was significantly less in anaesthetized dogs compared with nonanaesthetized dogs. Heart rate and respiration rates were well maintained but haemoglobin saturation decreased during first 6 minutes of anaesthesia. It was suggested that although significant decrease in mean weal size may not be clinically important but propofol has potential for use during intradermal skin testing in atopic dogs.

Muir and Gadawski (1998) reported dose dependent respiratory depression and apnea as the serious adverse effects of propofol anaesthesia.

Virtanen *et al.* (1998) studied the effect of propofol anaesthesia after premedication with medetomidine in dogs and found that the dogs reached a depth of anaesthesia in which there was no palpebral reflex on pain reaction. However, slight depression of circulatory and respiratory system was observed.

Heldmann *et al.* (1999) observed that animals receiving propofol were 3.8 times more likely to develop postoperative wound infection as compared with animals not given propofol.

Kwon *et al.* (1999) evaluated the effects of continuous administration of propofol in dogs and reported significant increase in

body temperature and respiration rate and non significant difference in total TLC, TEC and PCV values. The AST, ALT values were non significantly decreased while BUN and creatinine showed non significant changes.

Kim and Jang (1999) studied the effect of xylazine premedication on propofol anaesthesia and found that animals were recumbent immediately after propofol injection. No serious adverse effects were observed except vomiting after xylazine injection and insignificant ataxia during recovery. Body temperature, heart rate and respiratory rate were decreased significantly after propofol injection. No significant changes were observed in TLC, TEC, MCH and MCHC. AST, ALT, BUN, total proteins and albumin values were significantly increased. Premedication with xylazine could help to reduce the dose of propofol and incidence of adverse effects.

Redonodo *et al.* (1999) studied the effects of romifidine, medetomidine, and xylazine as premedicants with propofol-halothane-nitrous oxide anaesthesia in dogs and reported no significant changes in the pulse rate, respiration rate in all the three groups. However, mean arterial blood pressure, systolic pressure and diastolic pressure, while arterial oxygen saturation (SpO_2) was lower in medetomidine group, end tidal CO_2 (Et CO_2) was lower in romifidine group. Percentage of halothane necessary for maintaining anaesthesia was higher in xylazine group while it was lower in medetomidine or romifidine group. It was concluded

that combination of romifidine, atropine, propofol, halothane and nitrous oxide appears to be safe and effective drug combination for induction and maintenance of general anaesthesia in healthy dogs.

Patil *et al.* (1999) compared the efficacy of propofol and thiopental sodium as induction agent for inducing general anaesthesia in canines and reported that induction time did not differ significantly. However, significant difference in the duration of anaesthesia and recovery was noted between these groups. Recovery from propofol was extremely smooth and fast. However, blood pressure did not differ significantly between these groups.

Sarkate *et al.* (1999) used propofol successfully for induction and maintenance of anaesthesia in canines varying in age from one month to ten years. Various operations like spaying, leg amputation, dental fistula and pyometra were performed under propofol anaesthesia. No major and minor complications were reported either during anaesthesia or after recovery from anaesthesia in any case.

Batista *et al.* (2000) studied the intraocular pressure and partial carbon dioxide pressure in dogs after propofol injection and found non-significant changes.

Cortopassi *et al.* (2000) studied the effects of propofol premedicated with acepromazine or alfentanil and reported that acepromazine alone or acepromazine with alfentanil could be used as effective premedicants to

propofol anaesthesia. The induction and recovery from anaesthesia was smooth, uneventful and quiet, that permitted endotracheal intubation.

Kim and Kim (2000) evaluated acepromazine-ketamine combination and propofol for anaesthetic induction followed by maintenance by influrane in dogs and found that acepromazine-ketamine combination produced an increase in heart rate, rectal temperature and PaO_2, while propofol alone caused decrease in heart rate and rectal temperature. The respiration rate, systolic blood pressure, toe-web reflex and pH decreased in both the groups. Acepromazine-ketamine was found to be more suitable and useful than propofol as an induction agent for influrane anaesthesia in dogs.

Komar and Balicki (2000) studied the haemodynamic effects of atropine, medetomidine, propofol and atipamazole in dogs and reported that this combination caused increase in heart, arterial pressure, vascular resistance and decrease in cardiac output. After atipamezole injection, the cardiac output was increased but the arterial pressure, vascular resistance decreased five minutes after atipamezole injection, followed by increase in these parameters.

Lim *et al.* (2000) analyzed the effects of propofol at different dose rates after premedication with xylazine and reported rapid and smooth induction of anaesthesia. No vomiting and cyanosis were observed after induction and during propofol infusion. Haematological parameters viz. TEC, TLC, PCV and blood serum chemistry parameters (AST, ALT, BUN

and creatinine) showed non significant changes. Xylazine premedication provided an adequate anaesthesia for 90 min.

Lerche *et al.* (2000) studied the effects of propofol alone and propofol-ketamine combination for induction of anaesthesia in dogs and reported increase in heart rate after propofol-ketamine combination than propofol alone. Post induction apnea was more profound in propofol-ketamine anaesthesia while muscle twitching was observed in both the groups.

Grimm *et al.* (2001) studied the anaesthetic and cardiopulmonary effects of propofol premedicated with atropine, butorphenol and medetomidine and reported excellent anaesthesia accompanied by analgesia and good muscle relaxation. Heart rate decreased after medetomidine and propofol administration but returned to normal level after intravenous administration of atipamezole. Mild acidemia, hypercapnia, hypoxemia and decreased SaO_2 developed after premedication while PaO_2 and SaO_2 were further decreased by propofol injection. This combination was proved to be an effective anaesthetic protocol for minor surgical procedures in canines.

Murison (2001) reported that propofol was associated with frequent apnea, as compared to thiopentone anaesthesia. Time to first breath was significantly longer with propofol thiopentone and longest with the slow administration of propofol.

Raj *et al.* (2001) compared propofol and lipid free propofol anaesthesia in canines and performed various major and minor operations viz. tooth extraction, castration, pyometra, aural haematoma and mammary tumor successfully. The duration, quality of anaesthesia and degree of muscle relaxation were exactly similar with lipid and lipid free propofol anaesthesia. Xylazine-ketamine combination produced better quality of anaesthesia and muscle relaxation than the acepromazine-propofol combination.

Miller *et al.* (2002) used propofol (4 mg/kg I/V) in dogs premedicated with butorphanol tarterate (0.22 mg/kg IV), acepromazine maleate (0.05 mg/kg S/C) and glucopyrrolate (0.005 mg/kg S/C) to evaluate the effect of doxapram on the area of rima glottis (RG) successfully.

Material and methods

CHAPTER – III MATERIALS AND METHODS

3.1 Selection and Management of Animals:

To conduct this experiment fifteen healthy mongrel dogs of either sex, aging between 1 to 2 years and weighing between 10 to 15 kg were selected. These dogs were kept under hygienic and uniform managemental conditions.

In order to assess the normal health of these animals, samples of blood, urine and faeces were collected and analyzed. The body weight and rectal temperature of all the animals were recorded and the dogs that were free from parasitic infestations and whose blood picture and physiological parameters were within the normal range were included in this investigation. In the beginning de-worming was done with albendazole @ 5 mg/kg and during the experiment all the experimental dogs were kept in good health. Prior to each anaesthetic treatment, each dog was starved for 12 hrs. and water was withheld for the last 3 hrs.

3.2 Experimental Design:

The experiment was performed in three groups comprising of five animals in each group. Before the actual anaesthetic treatment, a pilot study was conducted for standardization of the dose and minimum effective dose was selected for the study.

Atropine sulphate[1] @ 0.04 mg/kg intramuscularly was administered to the animals in all the groups, 15 minutes before the treatment. The base values of physiological parameters were recorded and blood samples were collected for normal haematological and biochemical values. The animals were subjected to the following three treatments.

Group I- After Atropine sulphate premedication., Propofol[2] was be given @ 5 mg/kg body weight by slow intravenous injection.

Group II - Atropine sulphate premedication was followed by intramuscular injection of Acepromazine[3] @ 0.2 mg/kg body weight. This was followed 10 min. later by intravenous injection of propofol @ 5 mg/kg body weight.

Group III - Premedication was followed by intramuscular injection of Medetomidine4 @ 20 µg/kg body weight. This was followed 10 min. later by Propofol @ 5 mg/kg body weight intravenously.

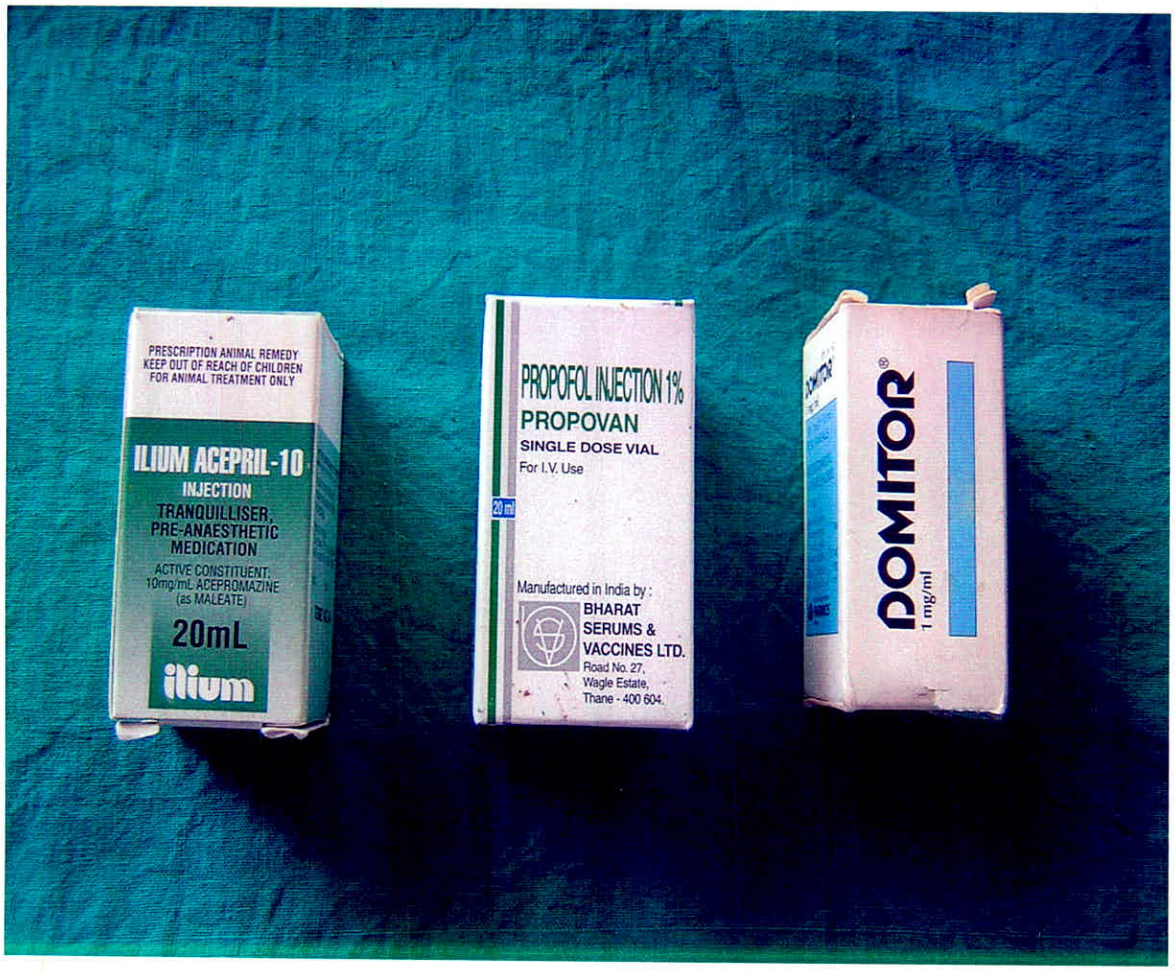
---

1. Atropine Sulphate – Alps Pharmaceuticals Co. Almora (Utteranchal)

2. Propovan – Bharat serums and vaccines Ltd. Thane – 400604

3. Acepril 10 – Troy Laboratories – Australia

4. Domitor – Orion Corporation – Finland.



Photograph-I. Showing the drugs used in the experiment.

3.3 Parameters studied

The different parameters that were studied in each group of animals after different treatment are as follows:

3.3.1 Clinical parameters : The following clinical parameters were assessed after different treatments -

a) **Onset of sedation / anaesthesia** – The onset of sedation / anaesthesia was noted as the duration between administration of anaesthesia and the dog eliciting a diminished response to external stimuli. The degree of sedation was graded as non-existing, slight, moderate and deep.

b) **Degree of analgesia** – It was assessed by presence or absence of pedal, pinprick, corneal, palpebral and conjunctival reflexes. Palpebral reflex was noted by taping the skin at the medial canthus of the eye or tuning the finger along the eyelashes while the pedal reflex was noted by pinching the web of the foot. To assess the corneal reflex, a gentle palpation of the lateral aspect of cornea was done. A reflex on a gentle prick of an inoculation needle on the medial aspect of the thigh was indicative of pinprick reflex.

c) **Duration of anaesthesia** – The time taken from the onset of anaesthesia till the return of pedal and pinprick reflexes in anaesthetized animal was recorded as duration of anaesthesia.

d) **Extent of muscle relaxation** – It was recorded by observing the tone of jaw muscles, flaccidity of tongue and relaxation of anal sphincter and it was graded as poor, good and excellent.

e) **Complete recovery** – The time interval between the onset of sedation / anaesthesia and the animal attaining its sternal recumbency was noted, as the time complete recovery time.

f) **Complications (if any)** – Various complications viz. nausea, vomition, salivation, lacrimation, muscle twitching etc. were recorded during and after anaesthesia in each group of animals if any.

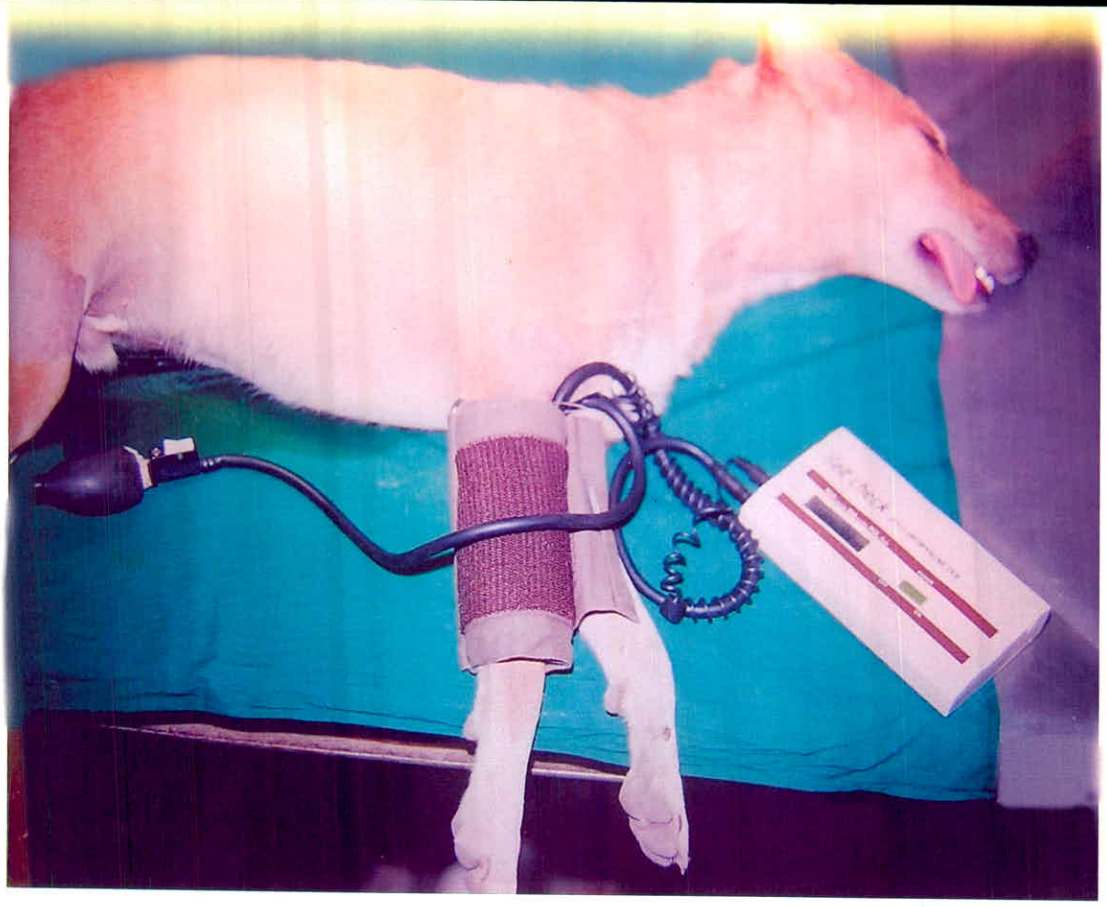
g) **Presence or absence** of **corneal, conjunctival, palpebral, pedal reflexes** and **relaxation of anal sphincter** were monitored.

3.3.2 Physiological parameters: This was comprised of recording the following parameters before and 10 min. after premedication and at 5, 15, 30, 60, 90 and 120 min. after anaesthesia.

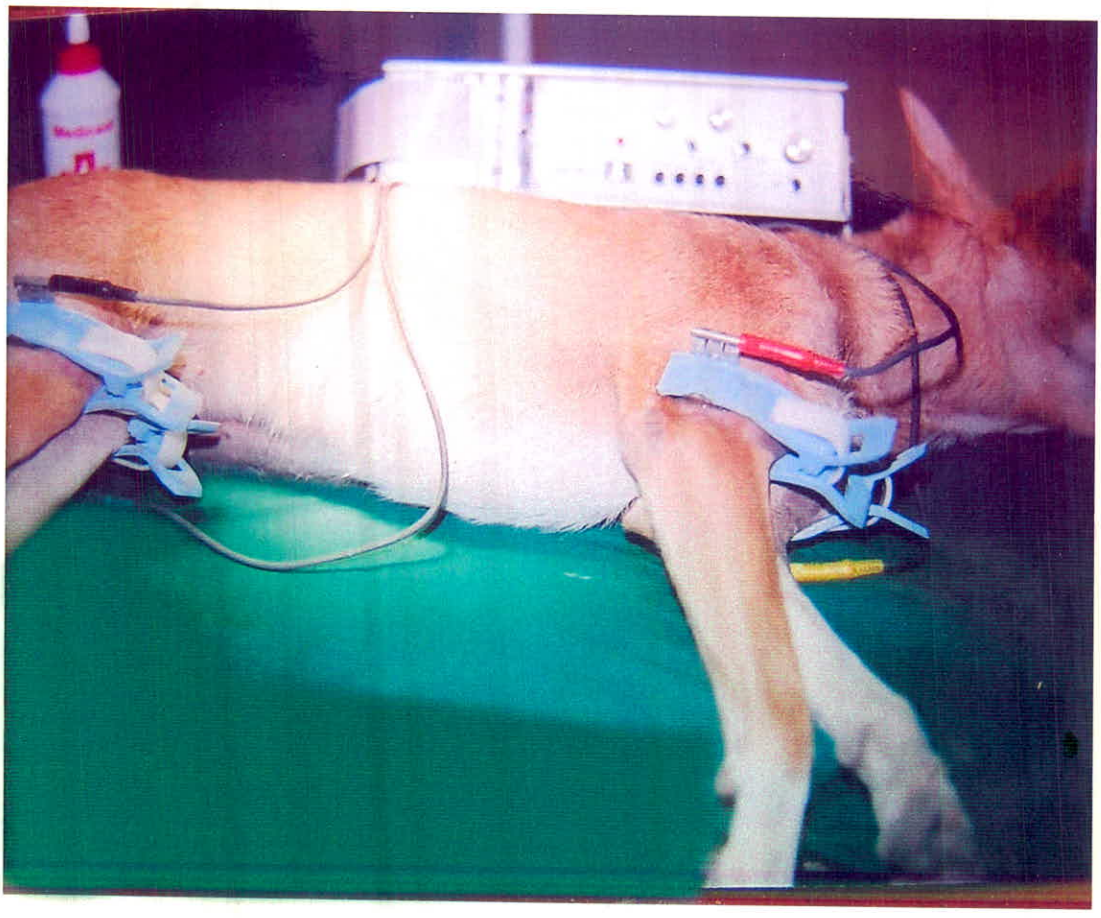
a) **Rectal temperature** – The rectal temperature was recorded with clinical thermometer and it was expressed in ^{0}F.

b) **Heart rate (per minute)** – The heart rate was recorded by auscultation with the help of stethoscope.

c) **Respiration rate (per minute)** – It was recorded by counting the thoracic respiratory movements per minute.



Photograph-II. Showing monitoring of blood pressure during anaesthesia by Electronic Sphygmomanometer.



Photograph-III. Showing monitoring of ECG during anaesthesia in different treatment group.

3.3.3 Cardiopulmonary parameters:

a) **Electrocardiogram** – The ECG was recorded by using "Cardiart 108T" (BPL). Electrocardiograph which was standardized at 1cm. equivalent to 1mv.and was recorded at a paper speed of 5, 10 and 25mm per second. It was analyzed for the duration and amplitude of P and T waves and mean QRS complex, PR interval and segment QT interval and ST segment. Plate electrodes were applied in the forearm and the lower thigh region with the animal in lateral recumbency. To ensure efficient contact of electrodes, after shaving the site electrode jelly was applied to the skin and the electrodes were held in place with latex rubber electrode straps.

b) **Systolic and diastolic blood pressure** - Arterial blood pressure was recorded by digital sphygmomanometer. The dog was restrained in lateral recumbency and the cuff was fixed to the forelimb just above the point of elbow.

These parameters were recorded before and 10 min. after premedication and at 5, 15, 30, 60, 90 and 120 minutes after the induction of anaesthesia.

3.3.4 Haematological parameters: Blood samples were collected from the experimental dogs before the premedication and at 60, 120 and 360 minutes after induction of anaesthesia. The venous blood (approximately 2.5-ml) was collected by veinpuncture either from

cephalic or tarsal vein in the vials containing ethylene diamine tetra acetic acid (EDTA). The study of following parameters was conducted as per the methods described by Jain (1996).

a) **Haemoglobin (g%)** – The haemoglobin concentration in the blood was estimated by Sahil's haemoglobinometer.

b) **Packed cell volume** – The PCV was estimated by Wintrobe's tube method.

c) **Total Erythrocyte Count (millions per cubic millimeter)** – The count was made with the help of Neubaur's counting chamber of haemocytometer.

d) **Total Leucocyte Count (Thousands per cubic millimeter)** – It was made with the help of Neubaur's counting chamber of haemocytometer.

3.3.5 Biochemical parameters: The serum samples from the dog were collected at 0, 60, 120 and 360 minutes to estimate the biochemical parameters. These parameters were estimated by standard procedures and by using semi-automated analyzer (ROBONIK-ASP 300). The parameters were as follows-

- **Serum glucose (mg/dl)**
- **Serum protein (g/dl)**

- **Blood urea nitrogen (mg/dl)**
- **Creatinine (mg/dl)**
- **AST (Unit/L.)**
- **ALT (Unit/L.)**

3.4 Clinico-Surgical study: Various surgical operations viz. gastrotomy, enterotomy, castration, spaying and correction of ear hematoma were performed by using above anaesthetic combinations to assess the suitability of these combinations for short and long term surgical procedures in canines.

S.No.	Operation	Group	No. of animals operated
1	Gastrotomy	III	2
2	Enterotomy	II	2
3	Spaying	III	2
4	Haematoma of ear	II	2
5	Castration	I	2
		Total:	10

3.5 Statistical Analysis: The mean and standard error of the recorded values were calculated. The data was analyzed by C.R.D. as per the procedure out lined by Snedecor and Cochran (1994).

Results

The present study was undertaken to compare the clinical, physiological, haematological, biochemical and clinico-surgical effects of acepromazine and medetomidine as premedicants to propofol anaesthesia in dogs and to evaluate the margin of safety while using these drugs for undertaking short term or long term surgical manoeuvres.

4.1 Clinical observations

4.1.1 Induction of anaesthesia:

The induction of anaesthesia in all the three groups are shown in Table I and represented in Fig.1.

The difference in the induction of anaesthesia was non-significant in all the three groups. However, in group II, where acepromazine was used as premedicant, the induction was smooth and quicker (0.43 ± 0.04 min) than in group I and III (0.51 ± 0.03 min. and 0.50 ± 0.01 min.) where propofol alone and medetomidine-propofol were used respectively. Emesis and vomition was observed in some of the dogs of group III where medetomidine was used as premedicant to propofol anaesthesia.

4.1.2 Duration of anaesthesia:

The duration of anaesthesia in all the three groups are shown in Table 1 and represented in Fig 2.

The mean duration of anaesthesia in medetomidine premedicated dogs of group III was found significantly ($P < 0.05$) longer (50 ± 5.7 min) in comparison to group I and group II (10.2 ± 0.8 and 24 ± 2.44 min respectively). In group III the quality of anaesthesia and extent of muscle relaxation were excellent to perform major surgical procedures. In group I and group II short surgical anaesthesia with good muscle relaxation was achieved which was suitable for short surgical procedures. Salivation was not observed in any of the groups during the period of anaesthesia.

4.1.3 Complete recovery from anaesthesia:

The complete recovery from anaesthesia in all the three groups have been shown in Table 1 and represented in Fig. 2.

The time taken for complete recovery from anaesthesia was significantly ($P < 0.05$) more in group III (100.6 ± 9.1 min.) as compared to group I and group II (25.0 ± 1.0 min. and 66.0 ± 4.1 min. respectively). There was significant ($P < 0.05$) difference in the complete recovery time in all the three treatment groups. The recovery was smooth, free from excitement and uncomplicated in all the three groups of animals.

4.1.4 Signs of anaesthesia:

In group I (atropine + propofol), the anal pinch reflex were fully abolished where as pedal, corneal and palpebral reflexes were sluggish. The animals remained in lateral recumbency. No salivation was noticed

Table 1. Effects on clinical parameters induction (onset), duration and complete recovery after injection of acepromazine or medetomidine as premedicants to propofol anaesthesia in dogs.

Parameters	Groups (n=5)		
	I	II	III
Induction of Anaesthesia (min.)	0.51 ± 0.03	0.42 ± 0.04	0.50 ± 0.02
Duration of Anaesthesia (min.)	10.2 ± 0.8	24 ± 2.44**	50 ± 5.7**
Complete recovery (min.)	25 ± 1.0	66 ± 4.11**	100.6 ± 9.61**

* $P<0.05$ = Significant at 5% level

** $P<0.01$ = Significant at 1% level

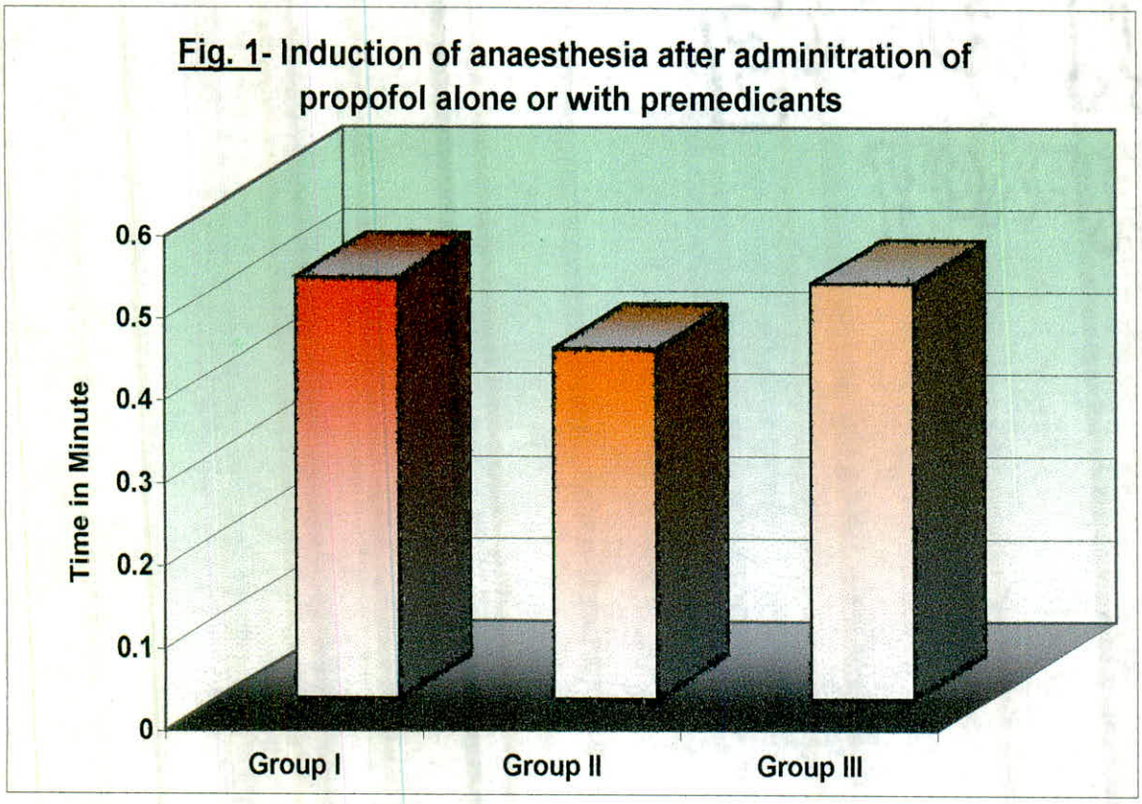


Fig. 1- Induction of anaesthesia after adminitration of propofol alone or with premedicants
Time in Minute
0.6
0.5
0.4
0.3
0.2
0.1
0
Group I
Group II
Group III

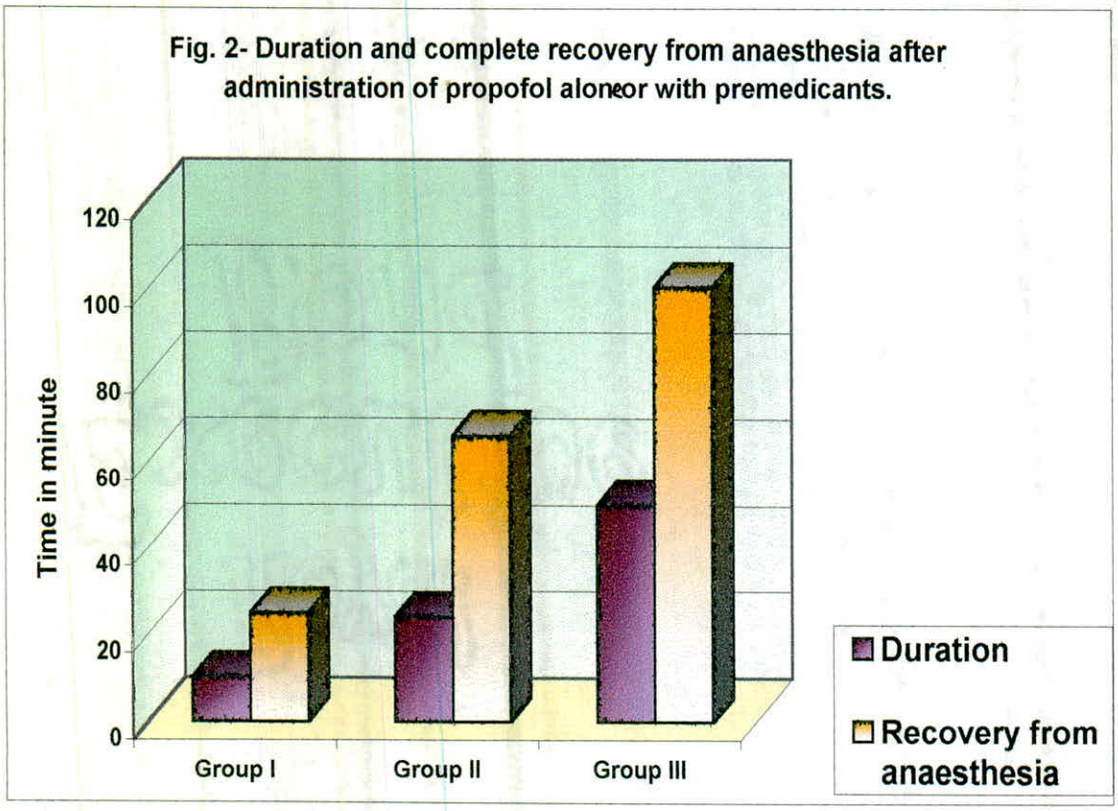
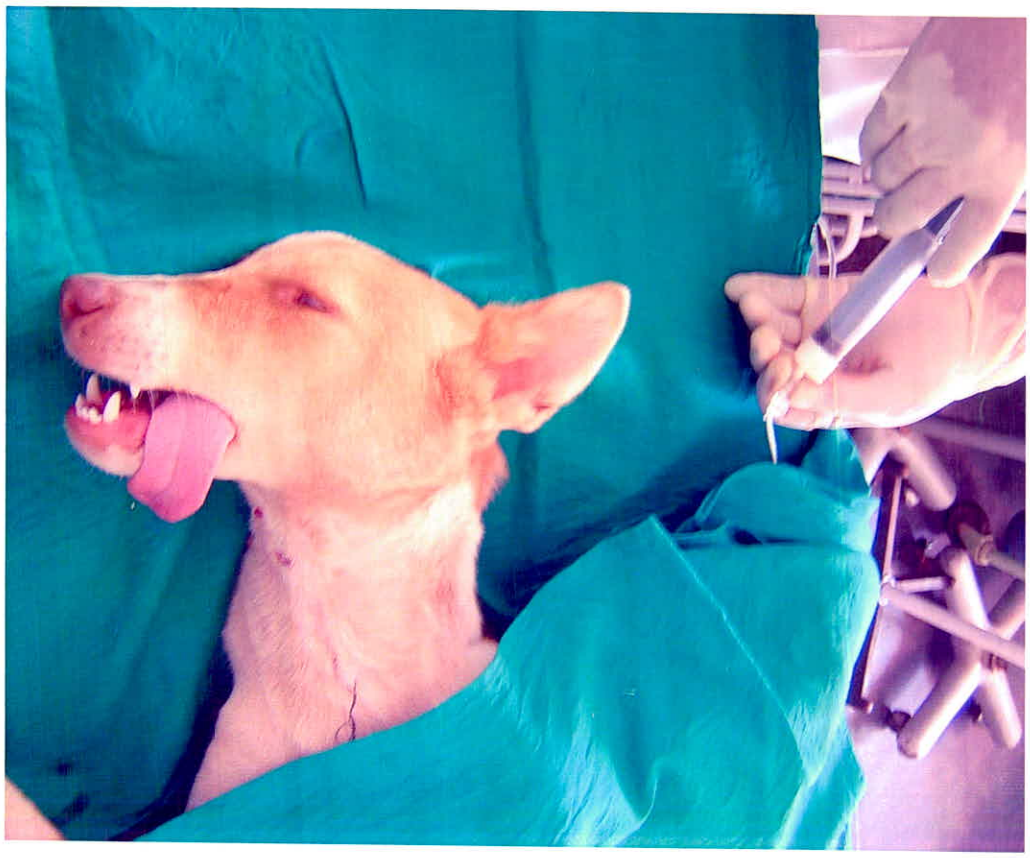


Fig. 2- Duration and complete recovery from anaesthesia after administration of propofol aloneor with premedicants.
Time in minute
120
100
80
60
40
20
0
Group I
Group II
Group III
Duration
Recovery from anaesthesia

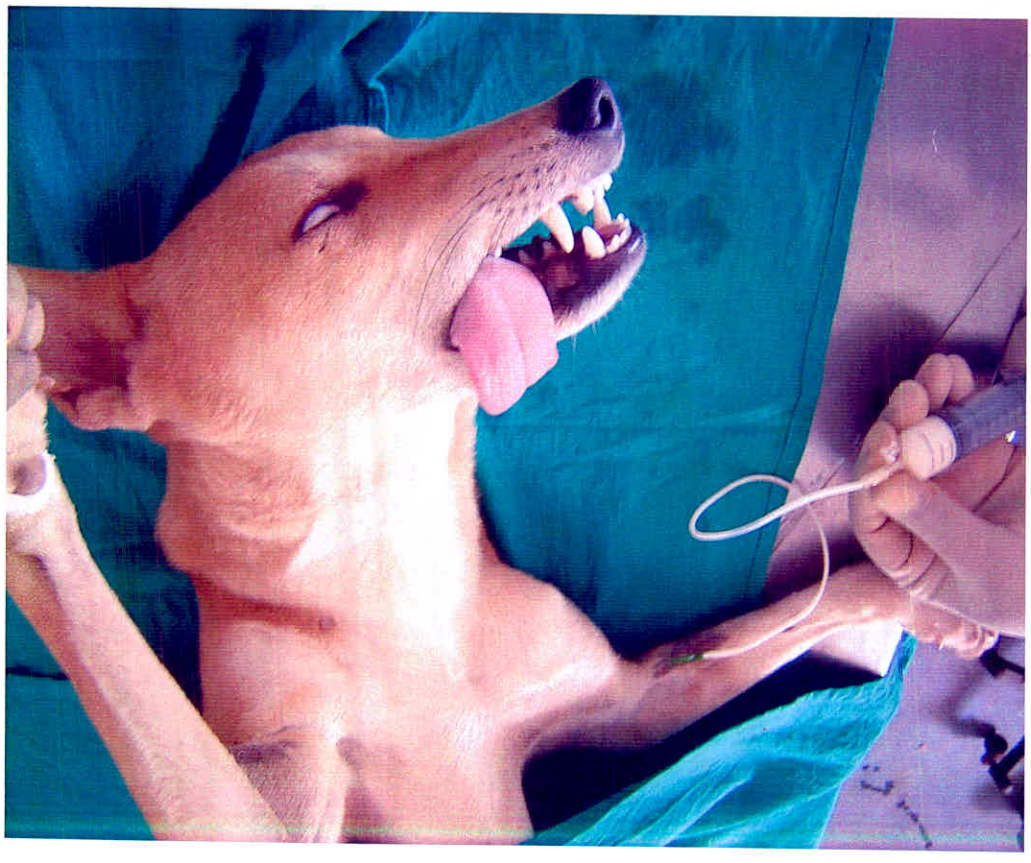
and eyes were open with dilated pupil. There was good analgesia and muscle relaxation for short duration. No hangover effect of drug was seen after complete recovery from anaesthesia.

In group II (atropine + acepromazine + propofol), the animals became recumbent after 5 to 8 min. of administration of acepromazine without showing excitement. The pedal, and anal reflexes were lost completely while corneal, palpebral and conjunctival reflexes were sluggish during the course of anaesthesia. Lacrimation and nasal discharge was observed in some of the animals during anaesthesia. Stiffness of neck and forelimbs was seen between 15 to 20 min. after the administration of anaesthesia in all the animals. Hallucination was seen in some of the animals at 20 min. post anaesthesia.

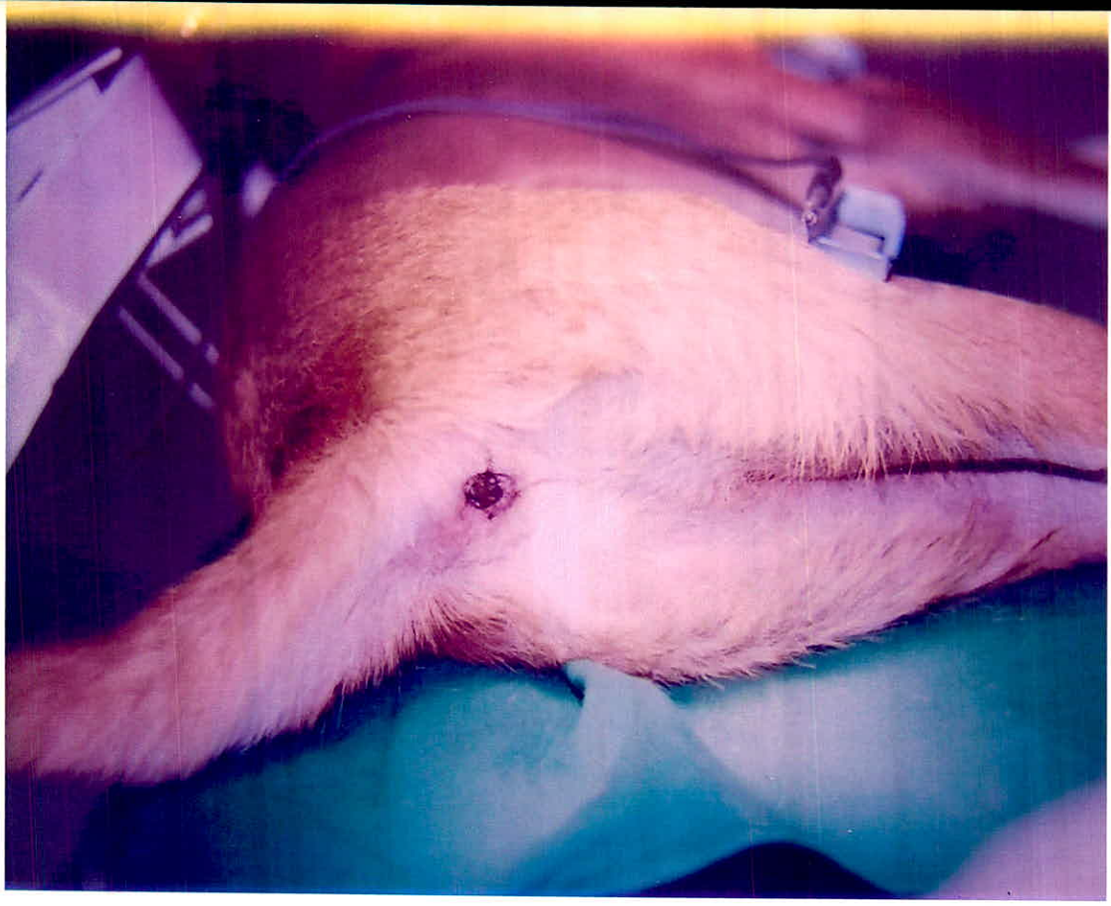
In group III (atropine + medetomidine + propofol), the induction was smooth. However, vomition was recorded in some of the animals after 7 to 10 min. after administration of medetomidine. The pedal, palpebral, conjunctival, corneal and anal reflexes were abolished while pharyngeal and laryngeal reflexes were depressed during the anaesthesia. The analgesia and extent of muscle relaxation was excellent for longer duration which was sufficient to perform major surgical procedures.



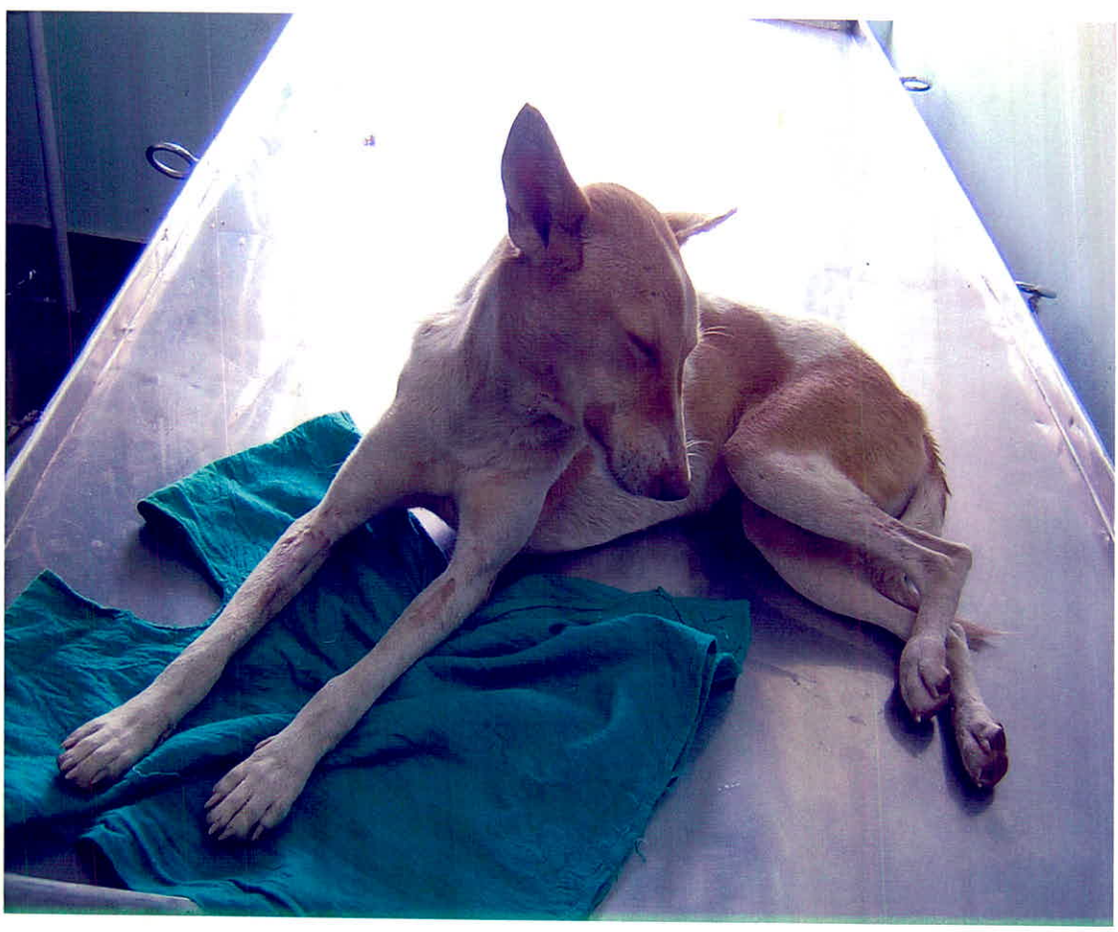
Photograph-IV. Showing injection of propofol and protrusion of tongue after induction of anaesthesia.



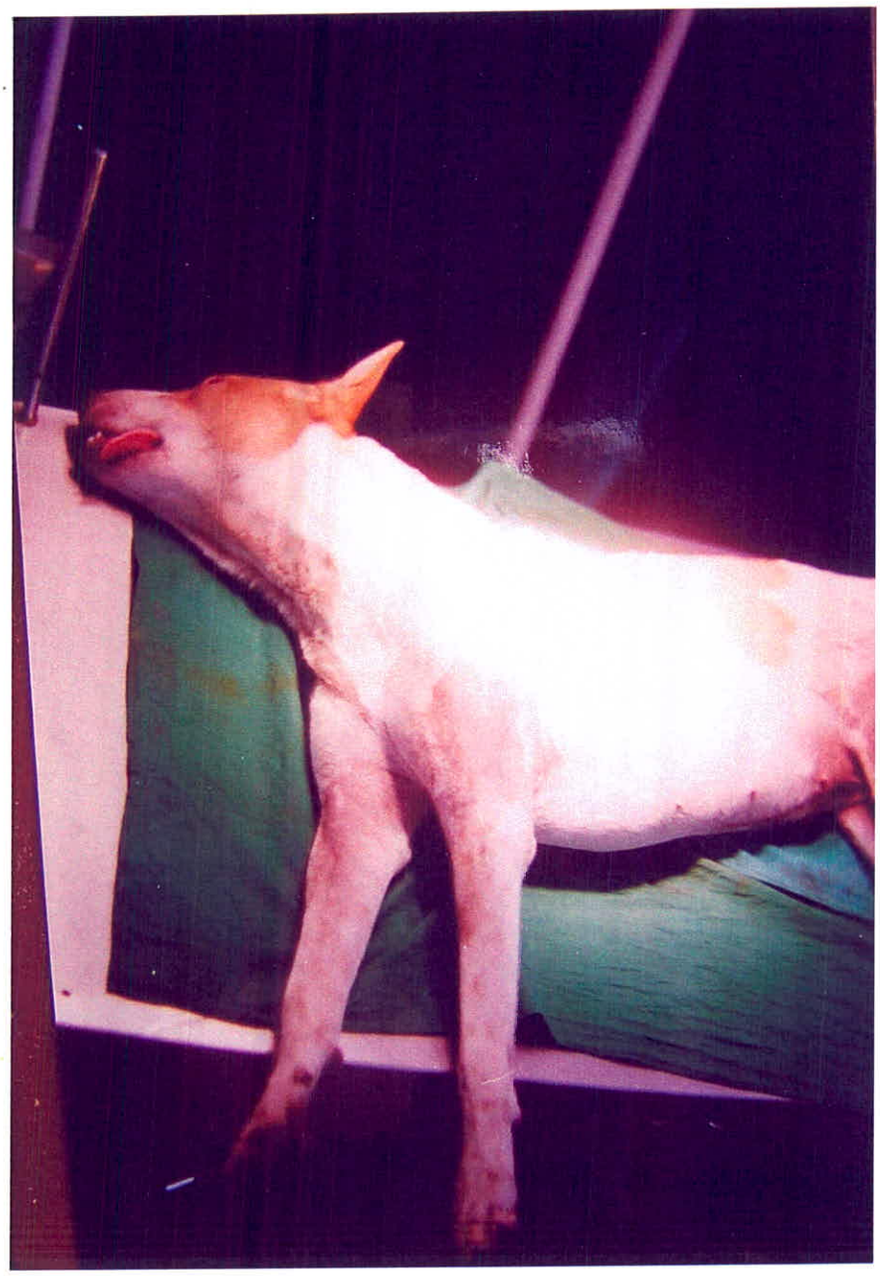
Photograph-V. Showing protrusion of tongue and abolition of eye reflexes during medetomidine-propofol anaesthesia.



Photograph-VI. Showing relaxation of anal sphincter during anaesthesia .



Photograph-VII. Showing the animal recovering from anaesthesia.



Photograph-VIII. Showing rigidity of limbs during acepromazine -propofol anaesthesia .

4.2 Physiological studies

4.2.1 Rectal temperature (°F):

The effect of propofol alone and alongwith administration of premedicants on rectal temperature are shown in Table 2. and represented in Fig. 3.

In group II and III there was slight increase in the rectal temperature 10 min. after administration of acepromazine and medetomidine as premedicants. Rectal temperature in all the three groups of animals was slightly decreased after administration of propofol. In group I, rectal temperature decreased up to 30 min. while in group II and III, it decreased up to 120 min. However, the changes were non significant in each time interval in all the three groups of animals.

4.2.2 Heart rate (per minute):

The mean values of heart rate after administration of propofol alone or in combination with acepromazine or medetomidine are shown in Table 2 and represented in Fig. 4.

A significant ($P< 0.01$) decrease in heart rate was observed 10 min. after the administration of acepromazine and medetomidine as premedicants in group II and group III respectively. The decrease in heart rate persisted up to 90 min. postanaesthesia in group II where as in group III the decrease in heart rate was significant up to 120 min. post anaesthesia. A significant ($P< 0.05$) decrease in heart rate was observed

Fig. 3 Effect on rectal temperature (°F) after injection of propofol alone or along with premedicants

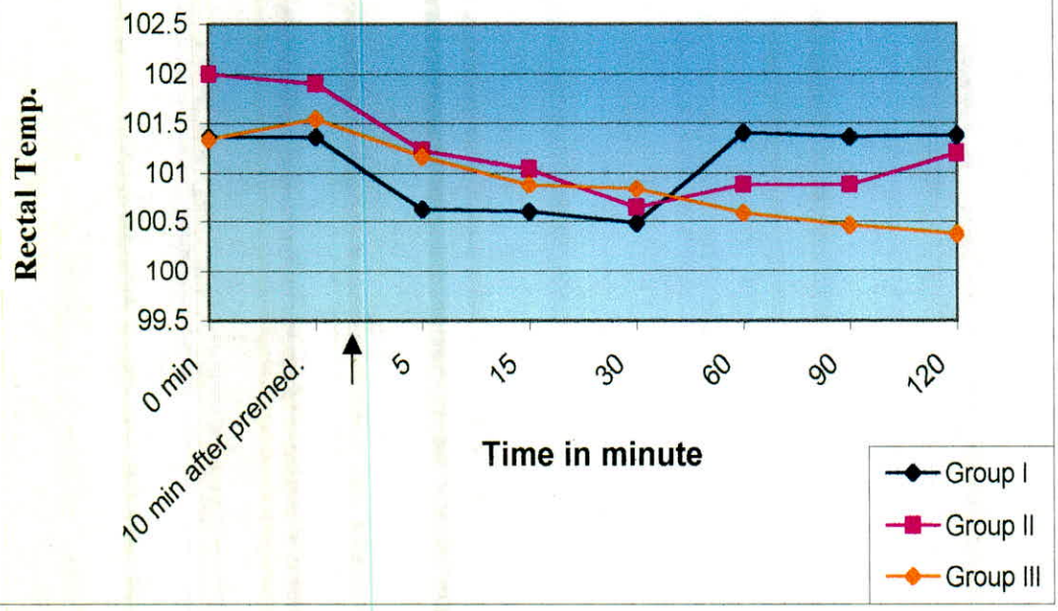
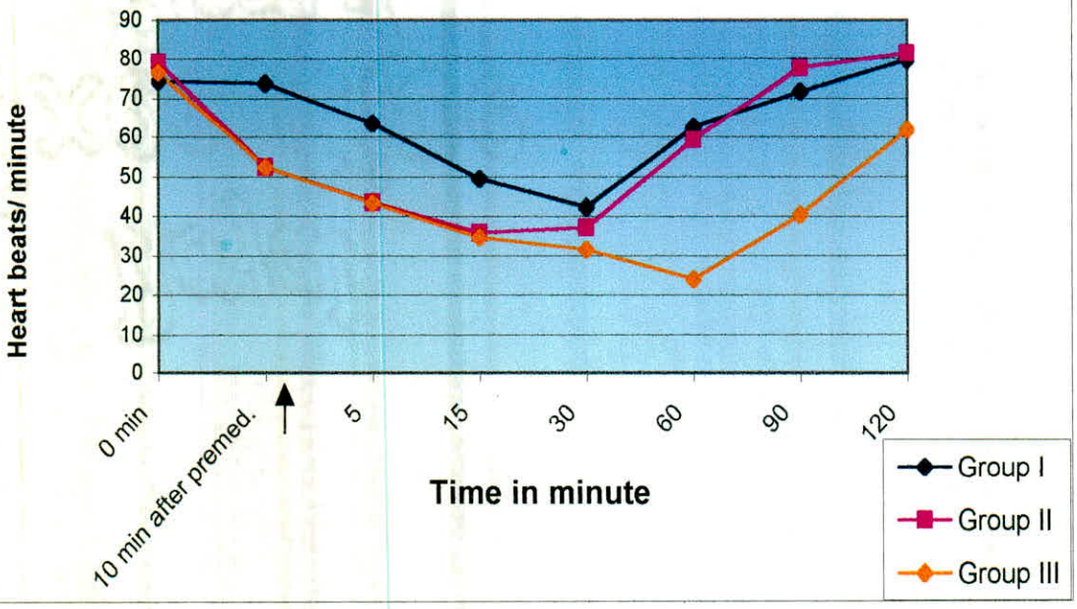


Fig. 4 Effect on heart rate after administration of propofol alone or with premedicants



between 5 to 60 min. post anaesthesia in group I which became highly significant (P< 0.01) between 15 to 30 min. postanaesthesia in response to administration of propofol alone.

The peak decrease in the heart rate was observed at 30 min. (42.4 ± 1.46 per min. from the control value of 74.4 ± 2.01 per min.) postanaesthesia in group I, at 15 min. (36.0 ± 1.81 per min. from the control value of 79.2 ± 1.88 per min.) in group II and at 60 min. (24.0 ± 1.14 per min. from the control value of 76.6 ± 1.32 per min.) in group III postanaesthesia.

4.2.3 Respiration rate (per minute):

The effect of propofol alone or in combination with acepromazine or medetomidine on respiration rate are shown in Table 2 and represented in Fig. 5

There was a non significant increase in respiration rate 10 min. after premedication in group I where atropine was used as a preanaesthetic. The animals of group II showed a significant (P< 0.05) decrease in the respiration rate between 5 to 30 min. post anaesthesia. After administration of propofol there was a significant (P< 0.01) decrease in respiration rate between 5 to 90 min. in group III where medetomidine was used as premedicant to propofol anaesthesia.

In three animals of group I, apnoea for 10 to 12 sec. was seen immediately after the administration of propofol followed by a decreasing trend of respiration was observed which became significant at 15 min.

Fig. 5 Effect on Respiration rate after injection of propofol alone or along with premedicants

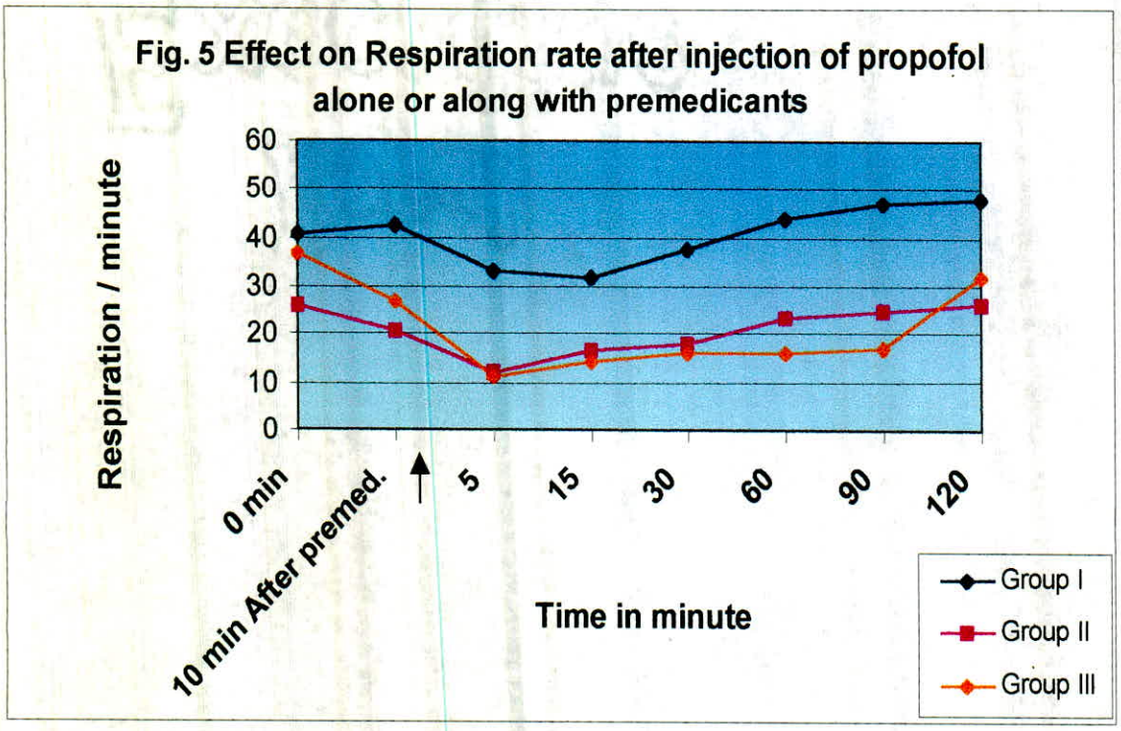


Table 2. Effects on physiological parameters after injection of acepromazine or medetomidine as premedicants to propofol anaesthesia in dogs.

Parameters	Groups (n = 5)	0 min.	10 min. after premedication	Post anaesthesia (minutes)					
				5	15	30	60	90	120
Rectal Temperature (^{0}F)	I	101.3 ± 0.26	101.3 ± 0.26	100.6 ± 0.3	100.6 ± 0.29	100.4 ± 0.36	101.4 ± 0.2	101.3 ± 0.22	101.3 ±0.17
	II	102 ± 0.12	101.9 ± 0.22	101.2 ± 0.29	101.0 ± 0.33	100.6 ± 0.48	100.8 ± 0.36	100.8 ± 0.41	101.2 ± 0.33
	III	101.3 ± 0.29	101.5 ± 0.2	101.1 ± 0.28	100.8 ± 0.32	100.8 ± 0.35	100.5 ± 0.54	100.4 ± 0.4	100.3 ± 0.38
Heart rate (Beats/min.)	I	74.4 ± 2.01	73.8 ±1.59	63.6 ±1.63*	49.6 ± 1.98**	42.4 ± 1.46**	62.6 ± 2.2*	71.8 ± 2.76	79.8 ± 4.88
	II	79.2 ±1.88	52.4 ±1.72**	43.6 ± 1.72**	36.0 ± 1.81**	37.2 ± 1.39**	59.4 ± 2.42**	77.8 ± 2.35	81.4 ± 1.28
	III	76.6 ± 1.32	54.2 ±1.56**	43.4 ± 2.31**	34.8 ± 2.13**	31.6 ± 1.2**	24.0 ± 1.14**	40.4 ± 1.2**	61.8 ±1.9*
Respiration (per min.)	I	40.8 ± 2.24	42.4 ± 1.46	33.0 ± 1.09*	31.6 ± 1.28*	37.8 ± 1.59	44.0 ±3.25	47.0 ± 3.09	48.0 ± 2.04
	II	26.0 ± 1.04	20.4 ± 0.74*	12.0 ± 1.37**	16.4 ± 1.5**	17.8 ±2.39**	23.4 ± 0.97	24.8 ±1.39	26.0 ± 2.09
	III	36.8 ± 4.72	27.0 ± 3.66	11.4 ± 2.4**	14.2 ± 3.07**	16.2 ± 2.31**	16.2 ± 2.05**	17.2 ± 3.21**	32.0 ± 4.03

* P<0.05 = Significant at 5% level

** P<0.01 = Significant at 1% level

then returned to normal by 30 min. In group II, a significant ($P< 0.01$) decrease in respiration rate was observed up to 30 min. postanaesthesia with maximum decreased value of 12.0 ± 10.7 per min at 5 min. thereafter it showed a steady increase and returned to normal by 120 min. The maximum decreased value in group III was 11.4 ± 2.4 per min. which was recorded at 5 min. postanaesthesia. There after it showed a gradual increase in respiration rate that returned to normalcy by 120 min.

4.2.4 Systolic blood pressure (mmHg):

The mean systolic blood pressure of the animals after premedication and anaesthesia at different intervals are shown in the Table 3 and represented in Fig. 6.

The animals of group I (propofol alone) showed a slight increase in the systolic blood pressure 5 min. after administration of propofol. This was followed by a significant ($P< 0.01$) decrease with the peak decreased value of 106.0 ± 1.37 mm Hg from the control value of 122.2 ± 2.69 mm Hg at 30 min post anaesthesia. However, the values returned to normalcy by 90 min. In group II and III, a significant ($P<0.01$) decrease was observed at 10 min. after the administration of acepromazine and medetomidine respectively. The peak decrease in the systolic blood pressure noted was 89.2 ± 2.31 mm Hg (control value 120.4 ± 1.02 mm Hg) and 76.6 ± 1.71 mm Hg (control value 119.2 ± 1.01 mm Hg) at 15 and 30 min in group II and III respectively. This was followed by a

Fig. 6 Effect on Systolic blood pressure (mmHg) after administration of propofol alone or along with premedicants

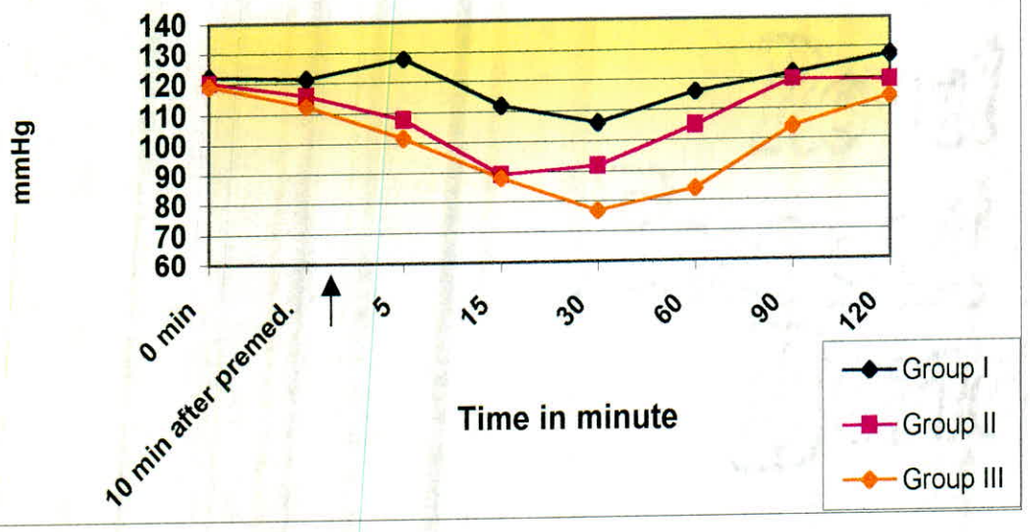


Fig. 7 Effect on Diastolic blood pressure (mmHg) after administration of propofol alone or along with premedicants

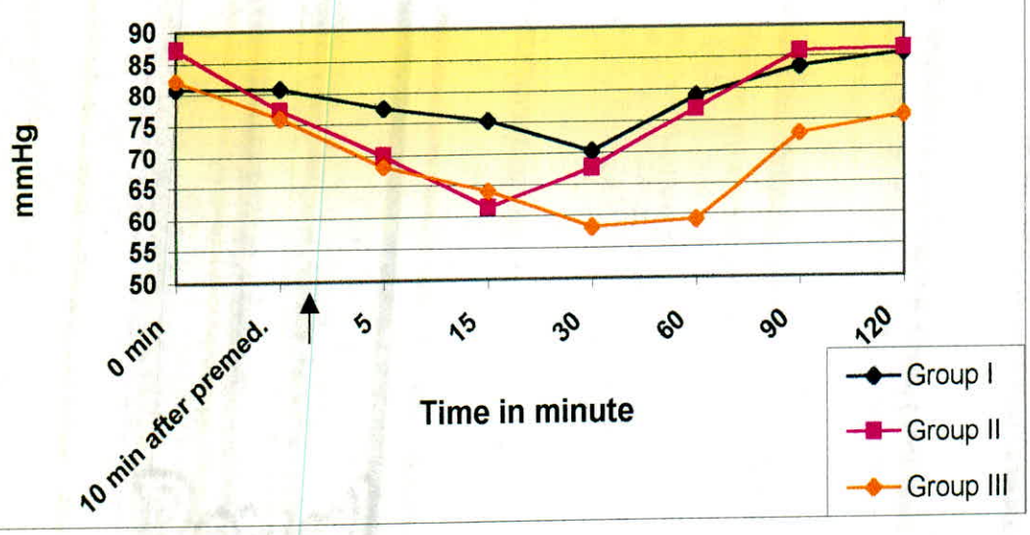


Table 3. Showing effects on systolic and diastolic blood pressure after injection of acepromazine or medetomidine as premedicants to propofol anaesthesia in dogs.

Parameters	Groups (n = 5)	0 min	10 min after premedication	Post anaesthesia (minutes)					
				5	15	30	60	90	120
Systolic blood pressure (mm Hg)	I	122.2 ± 2.69	121.4 ± 2.18	127.8 ± 1.95	111.8 ± 2.97*	106.0 ± 1.37*	115.8 ± 3.29	122.0 ± 1.58	127.6 ± 1.72
	II	120.4 ± 1.02	115.8 ± 1.42	107.6 ± 1.16**	89.2 ± 2.31**	91.8 ± 0.91**	104.8 ± 1.39**	119.8 ± 1.24	119.2 ± 0.86
	III	119.2 ± 1.01	112.4 ± 0.79*	101.6 ± 0.74**	88.0 ± 1.89**	76.6 ± 1.71**	84.0 ± 2.46**	104.0 ± 0.7**	113.8 ± 3.2
Diastolic blood pressure (mm Hg)	I	80.8 ± 1.59	80.8 ± 1.35	84.6 ± 1.86	75.2 ± 1.82*	70.2 ± 0.48*	79.0 ± 2.86	83.4 ± 1.72	85.4 ± 1.91
	II	87.2 ± 0.73	77.2 ± 1.01**	68.2 ± 1.68**	61.4 ± 1.93**	67.8 ± 2.22**	77.0 ± 1.14**	85.8 ± 1.01	86.2 ± 0.8
	III	82.2 ± 0.73	76 ± 1.41*	69.8 ± 1.35**	64.0 ± 1.3**	58.2 ± 2.00**	59.2 ± 2.59**	72.8 ± 1.56**	75.6 ± 1.83*

* $P<0.05$ = Significant at 5% level

** $P<0.01$ = Significant at 1% level

4.2.6 Electrocardiographic studies:

The electrocardiogram was used to study the rhythm, duration and amplitude of PQR, ST deflections of lead II. The duration and amplitude of PQR, ST deflections did not reveal any significant difference at various intervals in animals of group I and II. However, a slight increase in QRS duration and T wave amplitude in four animals of group III was seen which might be attributed to increase in ventricular depolarization brought about by medetomidine. There was an incomplete A-V block being observed in two animals of group III. Even the preadministration of atropine sulphate could not alleviate the undesirable effects.

4.3 Haematological observations

4.3.1 Haemoglobin (gm%):

The effects of various treatments in the level of haemoglobin are presented in Table 4.

Haemoglobin showed a non significant decrease after injection of propofol in group I and after medetomidine-propofol administration in group III at various intervals. These values ranged between 9.89 ± 0.26 gm% to 10.88 ± 0.46 gm%. In group II there was a non significant increase in the haemoglobin after acepromazine-propofol administration

which returned near normal level by 360 min. The values in group II ranged from 10.92 ± 0.38 gm% to 11.92 ± 0.31 gm% at various intervals.

4.3.2 Packed cell volume (%):

The effects of various treatments on packed cell volume are presented in Table 4.

The packed cell volume showed a non significant decrease in all the treatment groups at various intervals. It ranged from 34.56 ± 1.03 percent to 40.06 ± 0.36 percent in different groups at various intervals. These values returned to normal level at 360 min post anaesthesia in all the groups of animals.

4.3.3 Total erythrocyte count (millions/mm^3):

The effects of various treatments on total erythrocyte count are presented in Table 4.

In group I, there was slight but non significant decrease in the TEC where propofol alone was used, whereas the animals of group II and III, where acepromazine and medetomidine were used as preanaesthetic, there was non significant increase in the TEC values. However, the values returned near premedication values at 360 min. post anaesthesia. The TEC values ranged from 6.13 ± 0.21 millions/mm^3 to 8.68 ± 0.42 millions/mm^3 in all the three groups at various intervals.

Table 4. Effect on haematological parameters after administration of acepromazine or medetomidine as premedicants to propofol anaesthesia in dogs.

Parameters	Groups (n=5)	Time interval (minutes)			
		0	60	120	360
Hb (gm/dl)	I	10.47 ± 0.18	9.89 ± 0.26	10.20 ± 0.13	10.36 ± 0.16
	II	11.22 ± 0.42	11.92 ± 0.31	11.32 ± 0.18	10.92 ± 0.38
	III	10.92 ± 0.51	10.72 ± 0.49	10.88 ± 0.46	10.88 ± 0.46
PCV (%)	I	41.02 ± 0.57	40.04 ± 0.37	39.78 ± 0.35	40.06 ± 0.36
	II	35.10 ± 1.00	35.08 ± 0.74	34.76 ± 1.17	34.56 ± 1.03
	III	39.06 ± 1.11	38.08 ± 0.87	36.66 ± 1.00	38.08 ± 1.14
TEC ($\times 10^6$ cu mm^{-1})	I	6.52 ± 0.17	6.25 ± 0.20	6.13 ± 0.21	6.42 ± 0.18
	II	7.88 ± 0.23	8.68 ± 0.42	8.02 ± 0.32	7.80 ± 0.19
	III	6.92 ± 0.25	7.06 ± 0.14	6.82 ± 0.13	6.98 ± 0.04
TLC ($\times 10^3$ cu mm^{-1})	I	11.15 ± 0.31	11.32 ± 0.36	11.03 ± 0.31	11.11 ± 0.32
	II	11.46 ± 0.34	11.83 ± 0.18	11.27 ± 0.46	11.27 ± 0.40
	III	12.20 ± 0.36	11.86 ± 0.35	12.22 ± 0.20	11.84 ± 0.26

4.3.4 Total leukocyte count (thousands/mm^3):

The effects of various treatments on total leukocyte count are presented in Table 4.

A non significant increase in group I and II were observed which returned to the control values at 360 min. post anaesthesia. In group III, where medetomidine was used as preanaesthetic, a non significant decrease was recorded at 60 min. post anaesthesia which returned to near control values 120 min. after anaesthesia. The TLC values ranged from 11.03 ± 0.31 thousands/mm^3 to 12.22 ± 0.20 thousands/mm^3 in different group of animals at various intervals.

4.4 Biochemical studies

4.4.1 Glucose (mg/dl):

The changes in serum glucose level in response to different treatments at various time intervals are shown in Table 5 and represented in Fig. 8.

In all the groups there was increase in blood glucose at 60 min post anaesthesia which was non significant in group I, but significant ($P< 0.01$) in group II and III. The maximum increase in serum glucose level was observed at 120 min (107.54 ± 1.77 mg/dl from the control value 76.66 ± 2.91 mg/dl) in group II and (111.26 ± 1.45 mg/dl from the control value of 74.26 ± 2.19 mg/dl) in group III. The increase in the blood glucose level persisted up to 360 min. in group II and group III.

Fig. 8 Effect on Serum glucose (mg/dl) after administration of propofol alone or along with premedicants

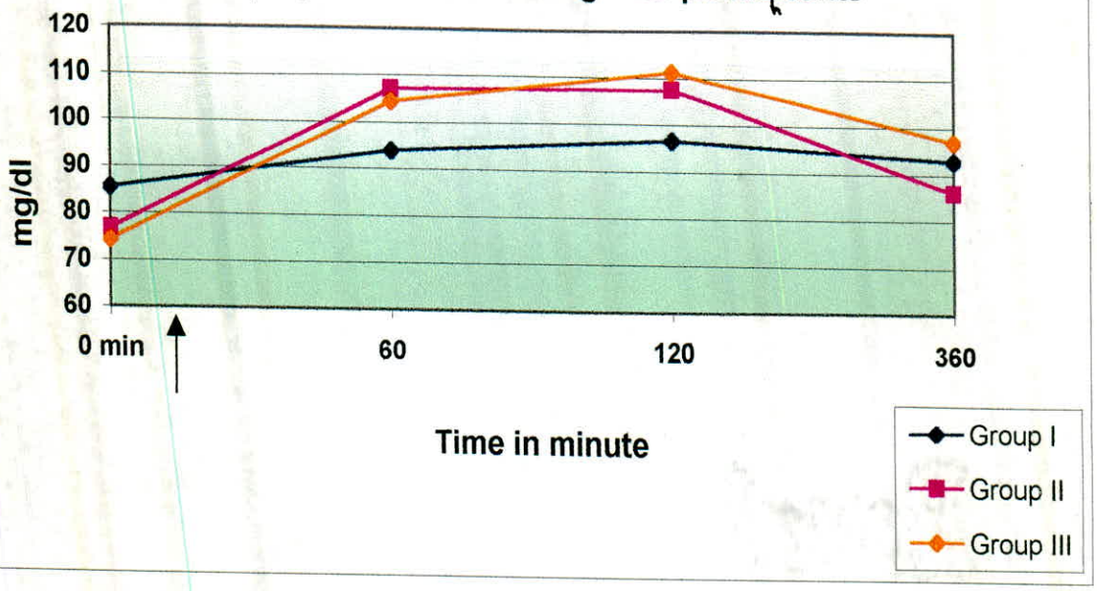
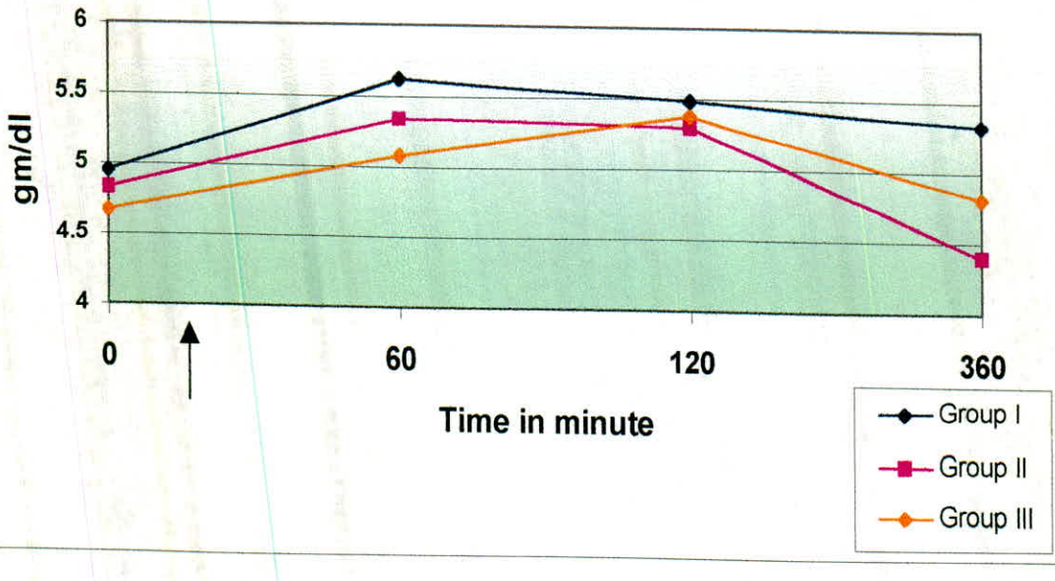


Fig. 9 Effect on Serum total proteins (gm/dl) after administration of propofol alone or along with premedicants



4.4.2 Total proteins (gm/dl):

The changes in the level of total proteins after different treatments at various intervals are shown in Table 5 and represented in Fig. 9.

There was a non significant increase in the level of total protein in all the group of animals between 60 to 120 min post anaesthesia. However, the values returned close to premedication level by 360 min in all the groups. The values ranged from 4.40 ± 0.16 gm/dl to 5.62 ± 0.11 gm/dl in different groups of animals at various intervals.

4.4.3 Serum urea nitrogen (mg/dl):

The effects of different treatments on serum urea nitrogen are shown in Table 5 and represented in Fig. 10.

Serum urea nitrogen showed a non significant increase between 60 to 120 min. after anaesthesia in all the three groups of animals. Thereafter, the values returned close to the preadministration level by 360 min post anaesthesia. The mean serum urea nitrogen values ranged from 19.40 ± 0.17 mg/dl to 23.92 ± 1.23 mg/dl in different groups of animals at various intervals.

4.4.4 Creatinine (mg/dl):

The mean serum creatinine level after various treatments are shown in Table 6 and represented in Fig. 11.

There was a non significant increase in serum creatinine level in group I with the maximum increased value of 1.44 ± 0.07 mg/dl from the control

Fig. 10 Effect on serum urea nitrogen (mg/dl) after administration of propofol alone or alongwith premedicants

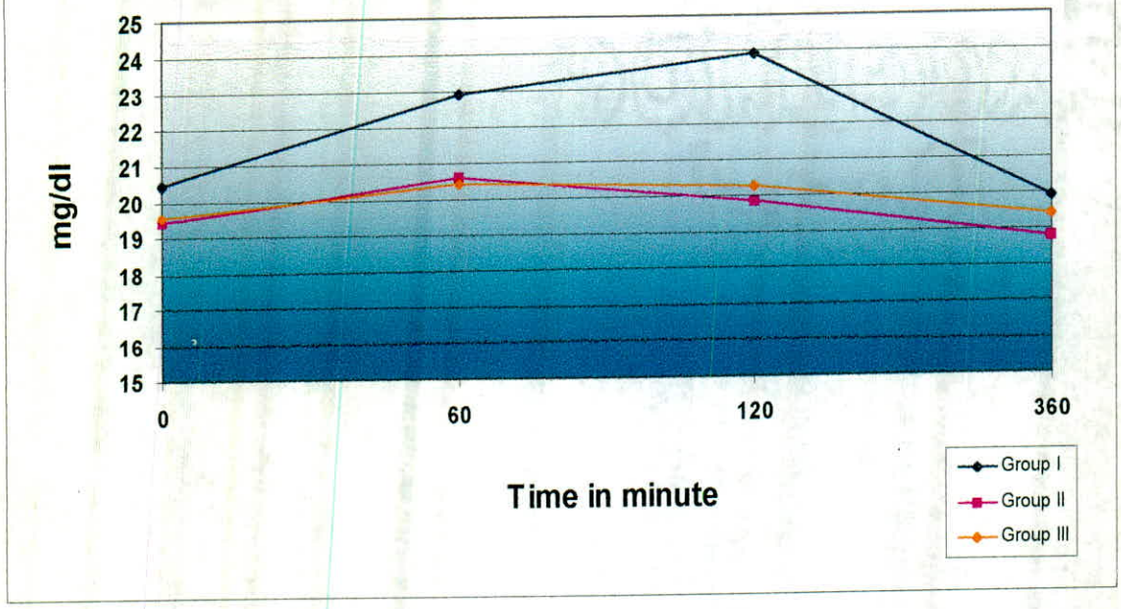


Fig. 11 Effect on serum creatinine (mg/dl) after administration of propofol alone or alongwith premedicants

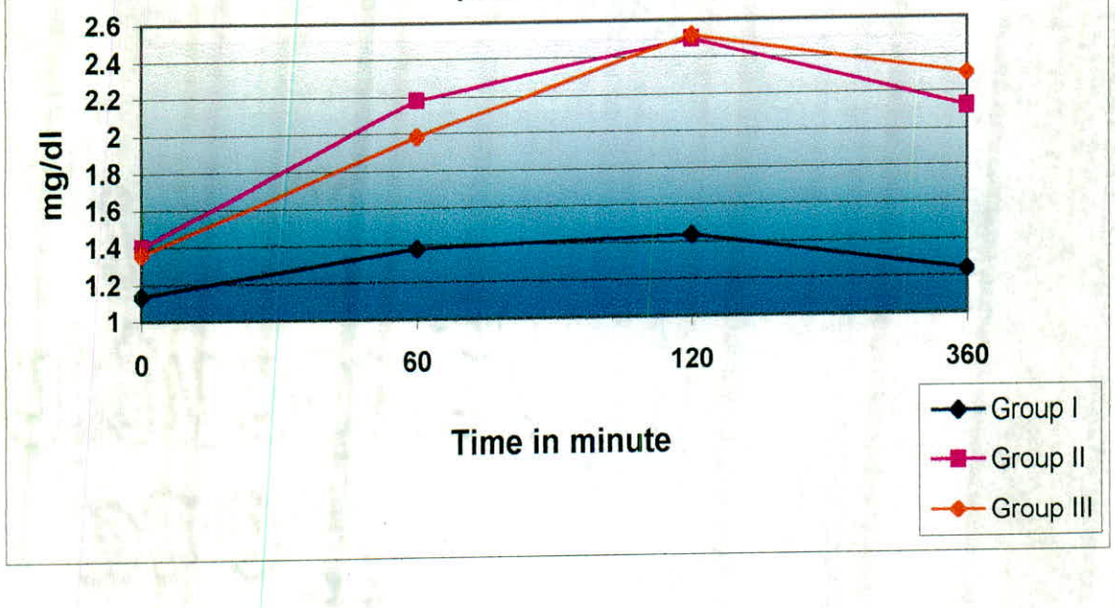


Table 5. Effect on biochemical parameters after administration of acepromazine or medetomidine as premedicants to propofol anaesthesia in dogs.

Parameters	Groups (n=5)	Time interval (minutes)			
		0	60	120	360
Glucose (mg/dl)	I	85.34 ± 2.86	093.72 ± 3.59	096.60 ± 3.43	92.94 ± 4.17
	II	76.66 ± 2.91	107.08 ± 2.60**	107.54 ± 1.77**	86.06 ± 3.12*
	III	74.26 ± 2.19	104.44 ± 3.07**	111.26 ± 1.45**	96.90 ± 1.01**
Total Proteins (gm/dl)	I	4.96 ± 0.16	5.62 ± 0.11	5.48 ± 0.31	5.32 ± 0.14
	II	4.84 ± 0.20	5.34 ± 0.10	5.30 ± 0.19	4.40 ± 0.16
	III	4.68 ± 0.16	5.08 ± 0.12	5.38 ± 0.22	4.80 ± 0.32
Serum Urea Nitrogen (mg/dl)	I	20.44 ± 1.65	22.90 ± 2.91	23.92 ± 1.23	19.90 ± 1.16
	II	19.42 ± 0.40	20.58 ± 0.56	19.84 ± 0.42	18.80 ± 0.37
	III	19.56 ± 0.27	20.40 ± 0.31	20.26 ± 0.17	19.40 ± 0.17

* $P<0.05$ = Significant at 5% level

** $P<0.01$ = Significant at 1% level

value of 1.14 ± 0.11 mg/dl at 120 min. post anaesthesia. In animals premedicated with acepromazine and medetomidine in group II and group III, there was a significant (P< 0.01) increase in serum creatinine level, which persisted up to 360 min. The maximum increased value of 2.50 ± 0.06 mg/dl (control value 1.40 ± 0.09 mg/dl) and 2.52 ± 0.05 mg/dl (control value 1.36 ± 0.09 mg/dl) were recorded in group II and III respectively.

4.4.5 Aspartate aminotransferase (U/L):

The mean aspartate aminotransferase (AST) activity after different treatments at various time intervals are shown in Table 6 and represented in Fig. 12.

The activity of AST in group I where propofol alone was used to induce anaesthesia, was found to be increased non significantly between 60 to 120 min. which was followed by a decrease to return to the preadministration level by 360 min. In animals of group II there was a significant (P< 0.05) increase in the activity of the enzymes at 60 min post anaesthesia. In animals of group III, there was a significant (P< 0.01) increase in the AST activity which persisted up to 120 min. post anaesthesia. Thereafter AST activity returned to normalcy 360 min. post anaesthesia in group III. In all the groups of animals the AST activity returned to pre injection level by 360 min. The maximum values recorded were 39.88 ± 1.55 U/L (control 33.92 ± 2.34 U/L) in group I, 43.62 ±

Fig. 12 Effect on AST (U/L) after adminisration of propofol alone or alongwith premedicants

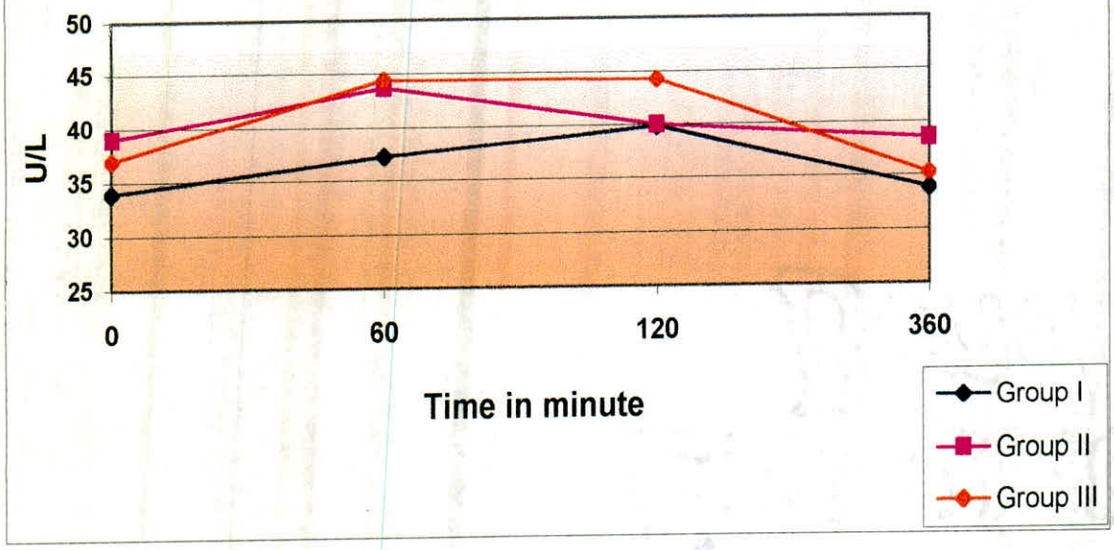


Fig. 13 Effect on ALT (U/L) after administration of propofol alone or alongwith premedicants

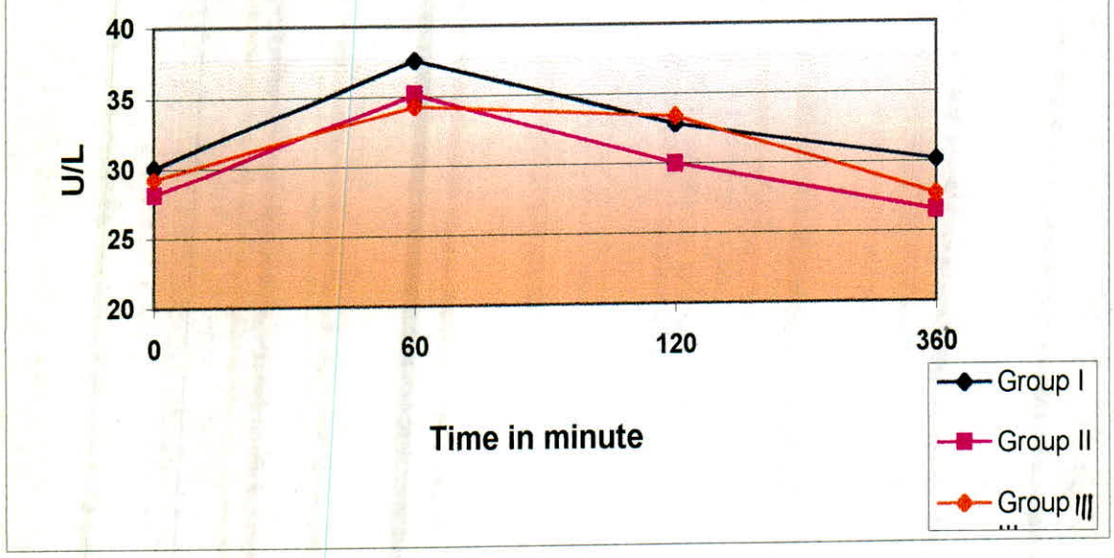


Table 6. Effect on biochemical parameters after administration of acepromazine or medetomidine as premedicants to propofol anaesthesia in dogs.

Parameters	Groups (n=5)	Time interval (minutes)			
		0	60	120	360
Creatinine (mg/dl)	I	1.14 ± 0.11	1.38 ± 0.11	1.44 ± 0.07	1.24 ± 0.06
	II	1.40 ± 0.09	2.18 ± 0.11**	2.50 ± 0.06**	2.12 ± 0.09**
	III	1.36 ± 0.09	1.98 ± 0.06**	2.52 ± 0.05**	2.30 ± 0.03**
AST (U/L)	I	33.92 ± 2.34	37.18 ± 1.82	39.88 ± 1.55	33.88 ± 2.56
	II	38.96 ± 0.92	43.62 ± 1.30*	40.00 ± 1.15	38.54 ± 0.90
	III	36.94 ± 0.74	44.40 ± 1.12**	44.26 ± 0.80**	35.28 ± 0.55
ALT (U/L)	I	30.06 ± 1.14	37.50 ± 3.37	32.92 ± 1.17	30.18 ± 1.64
	II	28.08 ± 0.69	35.16 ± 0.82*	30.00 ± 2.03	26.58 ± 0.94
	III	29.26 ± 0.33	34.28 ± 0.45*	33.46 ± 0.33	27.7 ± 0.52

* $P<0.05$ = Significant at 5% level

** $P<0.01$ = Significant at 1% level

1.30 (control 38.96 ± 0.92 U/L) in group II and 44.40 ± 1.12 U/L (control 36.94 ± 0.74) in group III.

4.4.6 Alanine aminotransferase (U/L):

The mean alanine aminotransferase (ALT) activity after different treatments at various time intervals are shown in Table 6 and represented in Fig. 13.

The ALT activity showed an increase in all the treatment groups at 60 min. post anaesthesia. The increase was non significant in group I where propofol was used alone to induce anaesthesia. In animals premedicated with acepromazine and medetomidine in group II and III, there was a significant ($P< 0.05$) increase in the activity of ALT 60 min. post anaesthesia. However, these values returned to premedication level by 360 min. The ALT values ranged from 26.58 ± 0.94 U/L to 37.50 ± 3.37 U/L in different groups at various intervals. The maximum values recorded in group II was 35.16 ± 0.82 U/L (control value 28.08 ± 0.69 U/L) and in group III was 34.28 ± 0.45 (control value 29.26 ± 0.33).

4.5 Clinico-surgical Effects:

The clinico-surgical effects after injection of acepromazine or medetomidine as premedicants to propofol anaesthesia in canines are shown in Table 7 and represented in photographs IX, X, XI and XII.

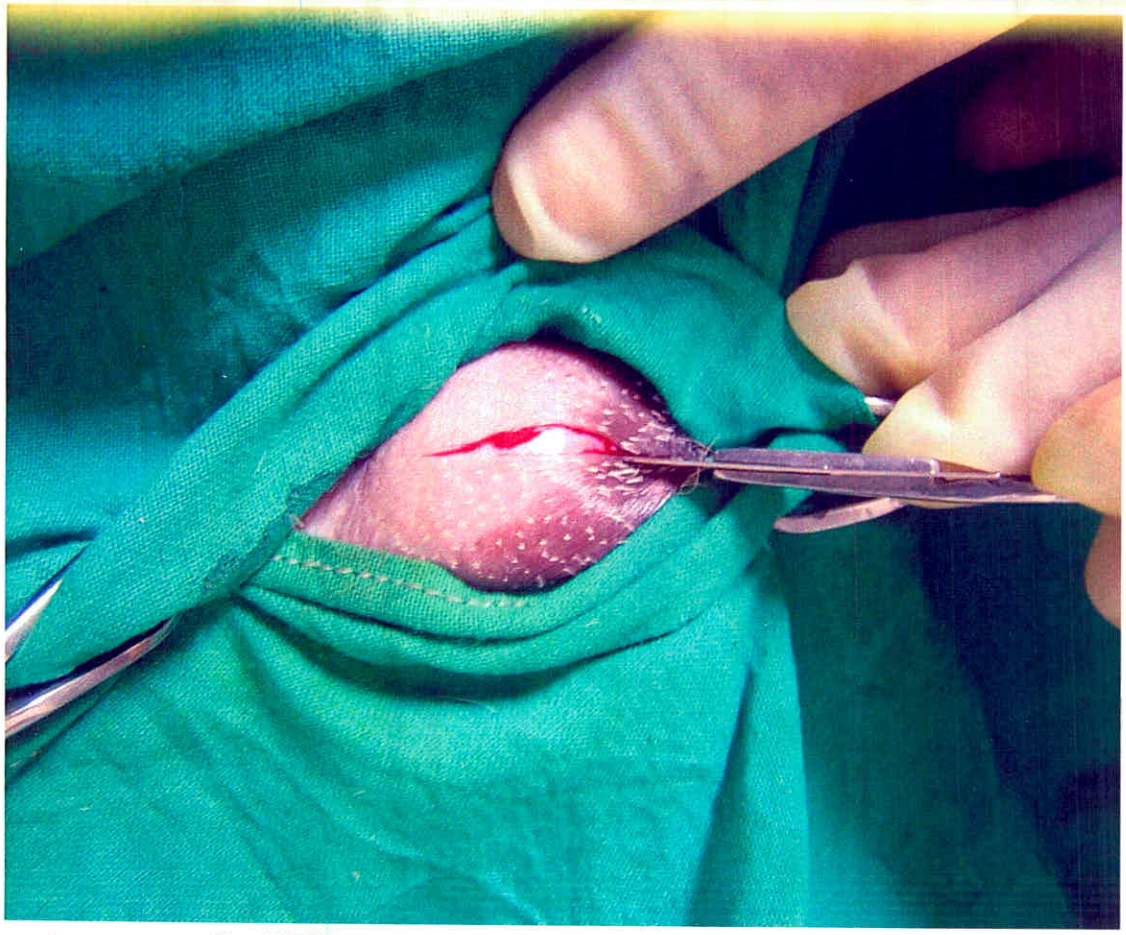
Various surgical operations were performed to assess efficacy of propofol as general anaesthetic alone or in combination with

acepromazine or medetomidine as premedicants to propofol anaesthesia in dogs. The induction of anaesthesia, duration, quality of analgesia, degree of muscle relaxation and complete recovery from anaesthesia were recorded. Various surgical operations (10) viz. gastrotomy, enterotomy, castration, spaying and haematoma of ear in dogs were performed under these anaesthetic-analgesic combinations. All operations were performed successfully under strict aseptic conditions and by using standard procedures. These operations were performed under single induction dose without maintenance by repeated dose of anaesthesia. The induction time varied from 25 to 35 sec. in three groups of animals after various treatments. Duration of anaesthesia ranged from 9 min. to 58 min. while complete recovery time ranged from 20 min. to 95 min. in various treatment groups. The combination of medetomidine and propofol caused excellent analgesia and muscle relaxation sufficient to perform major surgeries like gastrotomy, spaying in canines without any untoward effects during surgical intervention. Where as propofol alone and in combination with acepromazine produced short duration surgical anaesthesia with good quality analgesia and muscle relaxation. This combination was found suitable for short duration surgical procedures like castration, ear haematoma and enterotomy.

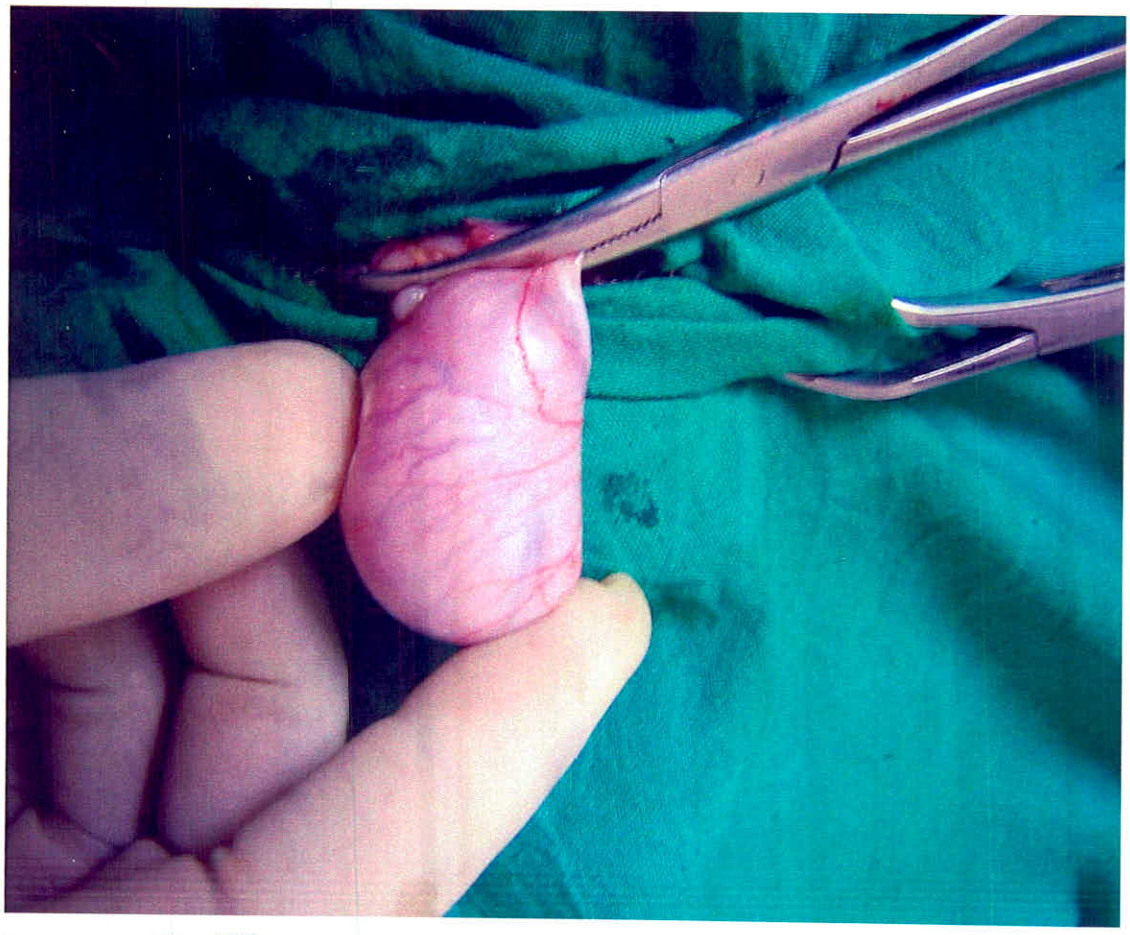
Table 7. Showing the clinico-surgical effects after injection of acepromazine or medetomidine as premedicant to propofol anaesthesia in canines during different surgical procedures

S. No.	Name of operation	No. of animal	Group	Induction time (sec.)	Duration of analgesia (min.)	Recovery (min.)	Extent of muscle relaxation	Overall grade of analgesia
1.	Gastrotomy	2	III	35	55	95	++++	Excellent
2.	Enterotomy	2	II	25	25	70	+++	Good
3.	Spaying	2	III	35	58	90	++++	Excellent
4	Haematoma of ear	2	II	30	23	65	+++	Good
5	Castration	2	I	30	9	20	+++	Good

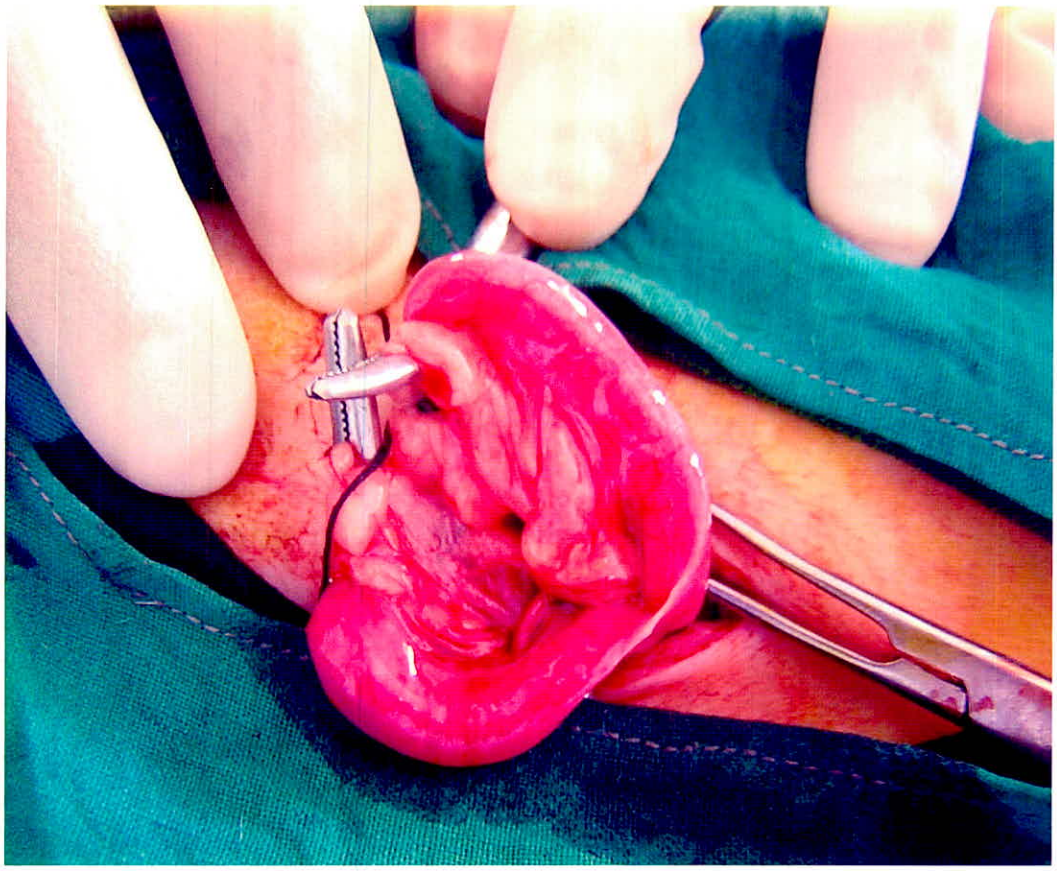
(-) = poor, (+) = mild, (++) = moderate, (+++) = good, (++++) = excellent.



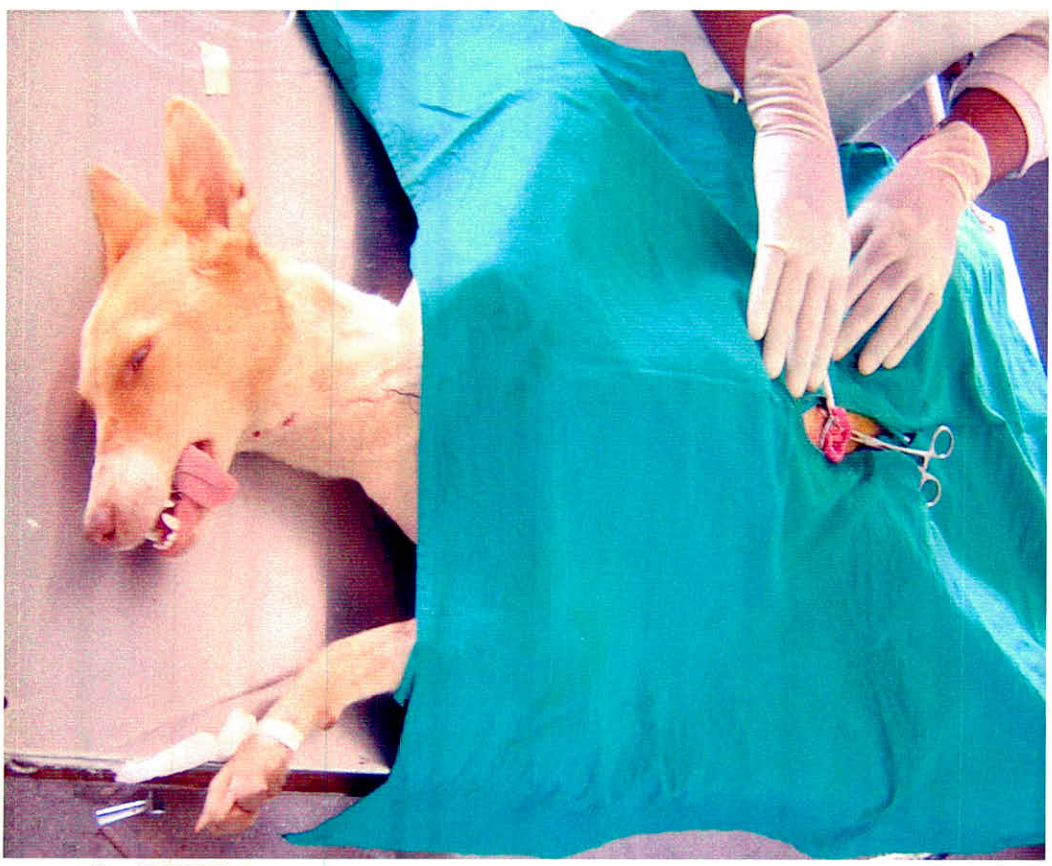
Photograph-IX. Showing incision above the scrotum for performing castration under propofol alone anaesthesia.



Photograph-X. Showing exteriorized testicle for castration under propofol alone anaesthesia.



Photograph-XI. Showing the magnified view of exteriorized uterine horns for performing ovariohysterectomy operation under medetomidine-propofol anaesthesia.



Photograph-XII. Showing the view of exteriorized uterine horns for performing ovariohysterectomy operation under medetomidine-propofol anaesthesia.

Discussion

The induction and maintenance of anaesthesia with intravenous agents has many potential advantages for the small animal practitioner because an intravenous technique is easy to manage and comparatively inexpensive apparatus is required (Watkins *et al.*, 1987). Emulsion preparation of propofol for intravenous anaesthesia was approved for use in human beings in the United States in 1989 and in dogs in 1996. In dogs propofol gave an excitement free induction with rapid and quiet recovery (Jane *et al.*, 1998). This drug can be administered as a single bolus dose for induction of general anaesthesia (Morgan and Legge, 1989) or to maintain anaesthesia by intermittent injections of propofol (Watkins *et al.*, 1987). Premedication with tranquilizers or sedatives reduces the dose of propofol required for anaesthesia (Cullen and Reynoldson, 1993).

The aim of this study was to evaluate the suitability of acepromazine and medetomidine as premedicant to propofol anaesthesia for short and long term surgical procedures in canines.

5.1 Clinical observations

5.1.1 Induction of anaesthesia:

The induction was quicker in group II, where acepromazine was used as a premedicant, (0.43 ± 0.04 min) than in group I and III (0.51 ± 0.03 min. and 0.50 ± 0.01 min.) where propofol alone and medetomidine-

propofol were used respectively. However, the difference in the onset of anaesthesia among the three groups was not significant. It showed that administration of acepromazine or medetomidine as a premedicant, did not affect the onset of anaesthesia. Similar findings have been reported by Bufalari *et al.* (1995) in dogs. Emesis and vomition was observed in two out of five dogs of group III where medetomidine was used as premedicant to propofol anaesthesia. Similar findings were reported by Cullen and Reynoldson (1993) while using xylazine and medetomidine as preanaesthetics to propofol anaesthesia.

5.1.2 Duration of anaesthesia:

The mean duration of anaesthesia in dogs of group III was found significantly ($P < 0.01$) longer (50 ± 5.7 min.) in comparison to group I and group II (10.2 ± 0.8min. and 24 ± 2.44 min. respectively). It showed that preanaesthetic administration of medetomidine significantly ($P < 0.01$) increased the duration of anaesthesia. However, administration of acepromazine slightly but significantly ($P< 0.05$) increased the duration of anaesthesia. Increase in duration of anaesthesia was correlated to additive effect of preanaesthetics with propofol in depressing the activity of the cerebral cortex. Cullen and Reynoldson (1997) also endorsed that premedicants prolonged the duration of propofol anaesthesia. The quality of anaesthesia and extent of muscle relaxation were excellent in group III to perform major surgical procedures. In group I and II, short surgical anaesthesia with good

muscle relaxation was produced which was suitable for surgical procedures of short duration.

Similar findings have been reported by Geel (1991) after use of acepromazine-propofol anaesthesia in dogs and David (1992) after administration of medetomidine-propofol anaesthesia in dogs.

5.1.3 Complete recovery:

The time for complete recovery from anaesthesia was significantly ($P < 0.01$) more in group III (100.6 ± 9.1 min.) as compared to group I and group II (25.0 ± 1.0 and 66.0 ± 4.1 min. respectively). Thus preanaesthetic administration of acepromazine and medetomidine prolonged the recovery time that might be due to the depressive action of the preanaesthetics on central nervous system. The shortest recovery time with propofol alone, revealed the faster rate of metabolic clearance of propofol from the body (Duke, 1995).

These findings are in agreement with the findings of Sarkate *et al.*, (1999), Patil *et al.*, (1999) and Cortopassi *et al.*, (2000) after administration of propofol alone and in combination with different preanaesthetics in canines.

5.1.4 Signs of anaesthesia:

Anal pinch reflex were fully abolished where as pedal, corneal and palpebral reflexes were sluggish in animals of group I given propofol alone.

The pedal, and anal reflexes were lost completely while corneal, palpebral and conjunctival reflexes were sluggish during the course of anaesthesia in group II animals given acepromazine-propofol. Lacrimation and nasal discharge was observed in some of the animals during anaesthesia. Muscle twitching and stiffness of neck and forelimbs was seen between 15 to 20 min. after the administration of anaesthesia in all the animals of group II. Hallucination was seen in some of the animals at 20 min. post anaesthesia. Similar findings have been reported by Thibaut *et al.* (2002) while using acepromazine-propofol anaesthesia in canines.

In group III, the induction was smooth. However, vomition was recorded in some of the animals between 7 to 10 min. after administration of medetomidine. Similar findings were reported by Yamashita *et al.* (2001) while using medetomidine-propofol anaesthesia in canines. The pedal, palpebral, conjunctival, corneal and anal reflexes were abolished while pharyngeal and laryngeal reflexes were depressed during the anaesthesia. The analgesia and extent of muscle relaxation in group III was excellent for longer duration which was sufficient to perform major surgical procedures. Loss of pedal reflex in all the animals of group II and III were indicative of third plane of surgical anaesthesia achieved by the animals of these groups.

5.2 Clinico-physiological studies

5.2.1 Rectal temperature:

Rectal temperature in all the three groups of animals was non significantly decreased after administration of propofol. The reduction in rectal temperature was attributed to decreased metabolic rate, depressed peripheral circulation and depression of thermoregulatory centers. Salunke *et al.* (2002) and Robertson (1993) observed similar findings and reported that the decrease in rectal temperature was probably due to an additive action of preanaesthetic and propofol. Carlson and Champmal (1981) while using propofol in canines opined that the decreased rectal temperature might be due to thermoregulatory depressant effect of propofol.

5.2.2 Heart rate:

A significant ($P< 0.05$) decrease in heart rate was observed between 5 to 60 min. post anaesthesia in group I which became highly significant ($P< 0.01$) between 15 to 30 min. postanaesthesia in response to administration of propofol alone. Similarly, in group II, a significant ($P< 0.01$) decrease in heart rate was observed 10 min after the administration of acepromazine which persisted up to 90 min. postanaesthesia. It might be due to propofol induced vasodialation leading to fall in systemic vascular resistance as well as dose related depression of myocardial contractibility (Duke, 1995).

A significant (P< 0.01) decrease in heart rate was observed 10 min after the administration of medetomidine as premedicant to propofol in animals of group III. The decrease in heart rate was significant up to 120 min. post anaesthesia. This might be due to direct action of α_2 agonist on the post synaptic receptors of the vascular smooth muscles leading to vasoconstriction and an initial transient hypertension followed by pronounced hypotension (Bufalari, 1998)

5.2.3 Respiration rate:

There was a non significant increase in respiration rate 10 min. after atropine premedication in group I followed by apnoea for 10 to 12 sec. immediately after the administration of propofol in 3 animal out of 5 animals of group I. Similar findings have been reported by Cullen and Reynoldson (1993), Salunke *et al.* (2002) using propofol alone and with medetomidine as premedicant. After that there was a decreasing trend of respiration, which become significant (P< 0.05) at 15 min. followed by return to normalcy by 30 min. post anaesthesia. The increase in the respiration recorded 10 min. after the administration of atropine sulphate may be due to the struggling of the animal and initial predominant action of the drug.

After combination of propofol with premedicants, a significant (P< 0.01) decrease in respiration rate was observed up to 30 min. in animals of group II and between 5 to 90 min. in group III premedicated with acepromazine and medetomidine respectivily. The decreased respiration

rate in group II and III, where acepromazine and medetomidine were used as preanaesthetics to propofol might be due to the direct depressant action of acepromazine and medetomidine on central nervous system in general and on respiratory center in particular. However, medetomidine has anaesthetic qualities with far less respiratory depression than narcotics (Bloor *et al.*, 1989).

The results of the present study are in agreement with Muir and Gadawski (1998) and Murison (2001) who reported dose dependent respiratory depression as the serious side effect of propofol anaesthesia.

5.2.4 Systolic and diastolic blood pressure:

The animals of group I showed a non significant increase in the systolic and diastolic blood pressure 5 min. after the administration of propofol followed by a significant ($P< 0.05$) decrease up to 30 min. post anaesthesia. Propofol has been reported to decrease nodal sinus activity, causing decreased blood pressure and heart rate in dogs (Quandt *et al.*, 1998). In group II and III, a significant decrease in systolic and diastolic blood pressure was recorded at 10 min. after the administration of acepromazine and medetomidine respectively. This was further decreased after administration of propofol and returned to normalcy at 120 min post anaesthesia. The results of the present study are in agreement with Thurmon *et al.* (1994). They suggested that administration of propofol helps to alleviate medetomidine induced vasoconstriction resulting in to decreased mean arterial blood pressure. Similar observations were

reported by Cullen and Reynoldson (1993), Bufalari *et al.* (1996) using medetomidine-propofol combination in dogs and Thibaut *et al.* (2002) using acepromazine-propofol combination in dogs. The decrease in the blood pressure under these anaesthetic regimens might be due to both, decrease in cardiac output and decrease in vascular resistance. However, the change in blood pressure was within clinically acceptable limits.

5.2.5 Electrocardiograph:

The administration of propofol alone and with premedication using acepromazine, did not cause much alterations in ECG. The duration and amplitude of PQR, ST deflection were observed within the normal limits in these two groups of animal (group I and II). The animals administered with medetomidine-propofol in group III showed a slight increase in QRS duration and T wave amplitude during the course of anaesthesia. However, it returned to normal level within 120 min. These might be due to increase in ventricular depolarization brought about by administration of medetomidine (Tiwari, 1996).

The results of this study are in agreement with the findings of Tiwari (1996) and Shinkar (2002) who also reported similar changes in ECG after administration of detomidine and attributed these ECG changes due to excessive stimulation of vagus nerve on account of parasympathomimetic action of medetomidine. Administration of medetomidine @ 20 µg/kg body weight did not show incomplete AV block

which might be due to vagolytic effect of atropine sulphate used as premedicant in this study.

5.3 Haematological studies

5.3.1 Haemoglobin:

Haemoglobin level showed a non significant decrease after injection of propofol in group I and after medetomidine-propofol administration in group III at various intervals. In group II there was a non significant increase in the haemoglobin 60 min. after acepromazine-propofol administration followed by a non significant decrease which returned near normal level by 360 min. The decrease in the haemoglobin level might be due to the splenic pooling of erythrocytes, which occurs with most of other anaesthetics. Similar findings have been reported by Lumb and Jones (1984) and Bayan *et al.* (2002). They observed a significant decrease in haemoglobin level during propofol anaesthesia with or without premedication.

5.3.2 Packed cell volume:

The packed cell volume showed a non significant decrease in all the treatment groups at various intervals. The decrease in PCV could be due to increase plasma volume during anaesthesia on account of vasodilation resulting in vascular pooling (Steffy *et al.*, 1976). David (1992) also reported a significant decrease in PCV percentage following propofol administration.

5.3.2 Total erythrocyte count and Total leukocyte count:

In group I, there was slight but non significant decrease in the TEC where propofol alone was used, whereas the animals of group II and III, where acepromazine and medetomidine were used as preanaesthetic, there was a non significant increase in the TEC values. However, the values returned near premedication values at 360 min. post anaesthesia.

A non significant increase in TLC values in group I and II were observed which returned to the control values at 360 min. post anaesthesia. In group III, where medetomidine was used as preanaesthetic, a non significant decrease in TLC was recorded at 60 min. post anaesthesia which returned to near control values 120 min. after anaesthesia.

These transient changes in TEC and TLC values might be attributed to stress of anaesthesia (Jain, 1986).

5.4 Biochemical studies

5.4.1 Serum glucose:

In all the group of animals, there was increase in blood glucose at 60 min post anaesthesia which was non significant in group I, but significant ($P< 0.01$) in group II and III. The increase in the blood glucose level persisted up to 360 min. in all the group of animals. It was non significant in group I, significant ($P< 0.05$) in group II where acepromazine was used as premedicant, and highly significant ($P< 0.01$)

in group III where medetomidine was used as premedicant to propofol anaesthesia.

The high rise in glucose level during anaesthesia might be attributed to decreased glucose utilization by the tissues, impaired insulin activity and increased blood concentration of adrenocortical hormones (Stark *et al.*, 1985). Similar findings have been reported by David (1992) and Bayan *et al.* (2002) after injection of propofol anaesthesia in dogs.

5.4.2 Total proteins:

There was a non significant increase in the level of total proteins in all the groups of animal between 60 to 120 min post anaesthesia. However, the values returned close to premedication level by 360 min in all the groups. This might be due to transient anaesthetic stress leading to rise in glucocorticoids which inturn might have led to slight rise in total protein levels. Similar findings have also been reported by Shinkar (2002) after administration of detomidine as premedicant to propofol anaesthesia in canines. Tiwari *et al.* (1994) also reported rise in serum total proteins after injection of diazepam-ketamine and xylazine-ketamine in dogs.

5.4.3 Serum urea nitrogen (SUN) and Creatinine:

Serum urea nitrogen showed a non significant increase between 60 to 120 min. after anaesthesia in all the three groups of animals.

Thereafter, the values returned close to the preadministration level by 360 min post anaesthesia.

There was a non significant increase in serum creatinine level in group I. In animals premedicated with acepromazine and medetomidine in group II and group III, there was a significant ($P< 0.01$) increase in serum creatinine level which persisted up to 360 min. post anaesthesia.

The rise in serum urea nitrogen and creatinine levels might be attributed to transient and temporary inhibitory effects of anaesthetic drugs on renal blood flow, which inturn might have caused a rise in serum urea nitrogen and creatinine. The results of the present study are in agreement with Kim and Jang (1999) and Lim *et al.*, (2000) after propofol anaesthesia in dogs premedicated with xylazine. Kwon *et al.* (1999) also reported a non significant increase in the SUN and creatinine levels after continuous administration of propofol anaesthesia in dogs.

5.4.4 Aspartate aminotransferase (AST) and Alanine aminotransferase (ALT):

The activity of AST in group I where propofol alone was used to induce anaesthesia, was found to be increased non significantly between 60 to 120 min. In animals of group II there was a significant ($P< 0.05$) increase at 60 min post anaesthesia. In animals of group III, there was a significant ($P< 0.01$) increase in the AST activity which persisted up to 120 min. post anaesthesia. In all the groups of animals the AST activity returned to pre injection level by 360 min.

The ALT activity showed an increase in all the treatment groups at 60 min. post anaesthesia. The increase was non significant in group I where propofol was used alone to induce anaesthesia. In animals premedicated with acepromazine and medetomidine in group II and III, there was a significant ($P< 0.05$) increase in the activity of ALT 60 min. post anaesthesia. However, these values returned to premedication level by 360 min.

The increase in the AST and ALT activities might be due to alteration in cell membrane permeability in response to haemodynamic changes by the anaeshtetic agents. However, increased activities of these hormones with in normal range indicates that, the vital organs like liver and kidneys were not affected by induction with propofol alone or after premedication with acepromazine or medetomidine in dogs. The results of the present study are in agreement with Dundee and Wyant (1988); Bowman (1989) and Bayan *et al.* (2002) after induction of propofol anaesthesia in dogs.

5.5 Clinicosurgical studies:

The effect of propofol as general anaesthetic alone or in combination with acepromazine or medetomidine as premedicants in dogs was judged by performing various surgical operations viz. haematoma of ear, castration, gastrotomy, enterotomy and spaying.

During the surgery, the animals remained calm and quiet in all the groups. These findings are in agreement with Bufalari (1998) who

confirmed that propofol was a safe and effective anaesthetic, suitable for a wide range of applications in dogs, when used alone or in combination with sedatives or analgesics.

Among these combinations, medetomidine-propofol combination was considered to be the best as it produced excellent analgesia and muscle relaxation. Vaisanen *et al.*, (2002) also reported that medetomidine may offer some advantage over acepromazine with respect to the ability to decrease perioperative concentrations of stress related hormones. So it was useful to perform major surgeries under this combination. However, the analgesia and muscle relaxation in group I and II was moderate and good respectively but was of short duration. There fore, minor or short surgical procedures were performed under these anaesthetic combinations.

Summary, Conclusion & Suggestions

SUMMARY

The present study was conducted on 15 mongrel dogs of either sex, aging between 1-2 years and weighing between 10-15 kg. The animals were kept under hygienic and uniform managemental conditions and observed for 10 days. Analysing blood, urine and faecal samples was done to assessed the normal health of the animals. All the dogs were dewormed and randomly divided in to three groups consisting of 5 dogs each. Prior to anaesthetic treatment, each dog was starved for 12 hrs. and water was withheld for the last 3 hrs. Atropine sulphate @ 0.04 mg/kg body weight I/M was given to the animals of all the groups 15 min. before each treatment.

In group I, propofol was administered @ 5 mg/kg body weight. In group II and III acepromazine @ 0.2 mg/kg body weight I/M and medetomidine @ 20 μg/kg body weight I/M respectively were administered as preanaesthetic, 10 min. prior to propofol administration.

Induction time, duration of anaesthesia and complete recovery from anaesthesia was evaluated and compared in all the three group of animals. The physiological and cardiopulmonary parameters viz. rectal temperature, heart rate, respiration rate, systolic and diastolic blood pressure and ECG changes were recorded before anaesthesia, 10 min. after premedication and at 5, 15, 30, 60, 90 and 120 min. postanaesthesia. Blood samples were collected before premedication and

at 60, 120 and 360 min. after induction of anaesthesia for haematological and biochemical studies. Ten operations were performed after induction of anaesthesia using propofol alone or with preanaesthetic viz. acepromazine and medetomidine to judge the suitability of different anaesthetic combinations for performing surgery in canines.

Induction of anaesthesia was rapid and smooth in all the animals of the three treatment groups. The duration of anaesthesia was significantly longer in group II and III as compared to group I. The quality of analgesia and degree of muscle relaxation was excellent in group III, better in group II and good in group I. No post anaesthetic complications were observed during the anaesthetic period except stiffness of neck and forelimbs between 15 to 20 min. post anaesthesia in group II. Complete recovery from the anaesthesia was smooth and uneventful in all the animals. However, hallucination was seen in some of the animals of group II during recovery from the anaesthesia.

Respiration rate, systolic and diastolic blood pressure showed a significant decrease in all the group of animals. However it was less significant in group I. The heart rate decreased significantly in all the group of animals but the rectal temperature was decreased non significantly. Electrocardiogram did not show any significant difference in the duration and amplitude of PQR, ST deflections in group I and II.

However, in group III, QRS amplitude and T wave showed deflections, but these changes were within clinically acceptable limits.

The heamatological parameters viz. total erythrocyte count, total leukocyte count, packed cell volume and haemoglobin concentration did not show any significant changes in all the three groups at various time intervals.

Serum glucose and creatinine showed a significant increase in animals of group II and III while total proteins and SUN values did not differ significantly in all the groups of animals. There was a significant increase in AST values observed in animals of group III. The animals of group II also showed less significant increase at 60 min. post anaesthesia. The ALT values also showed a significant increase at 60 min. post anaesthesia in group II and III.

Various surgical operations viz. haematoma of ear, castration, spaying, gastrotomy and enterotomy were performed successfully under these preanaesthetic-anaesthetic combinations. The sedation, analgesia and muscle relaxation was excellent in group III along with duration of anaesthesia sufficient to perform major surgical procedures. In the animals of group I and II, short duration surgical anaesthesia with good analgesia and muscle relaxation was produced which was sufficient to perform minor surgical procedures.

CONCLUSIONS

On the basis of this study the following conclusions were drawn-

1) Propofol (5 mg/kg body weight I/V) alone could be used safely for induction and maintenance of anaesthesia with good analgesia, muscle relaxation and the duration sufficient for short surgical procedures in canines.
2) Preanaesthetic injection of acepromazine (0.2 mg/kg body weight I/M) prior to induction of propofol anaesthesia was proved to be safer and better for undertaking minor surgeries but only care should be taken between 15 to 20 min. post anaesthesia during which stiffness of neck and forelimbs takes place.
3) Preanaesthetic administration of medetomidine (20 µg/kg body weight I/M) prior to administration of propofol anaesthesia produced excellent analgesia and muscle relaxation. The duration of anaesthesia was sufficient to perform major surgeries.
4) Recovery from the anaesthesia in all the anaesthetic combinations was smooth, free from excitement and uncomplicated in all the animals thus minimizing the chances of postanaesthetic complications.
5) The transient physiological, cardiopulmonary and biochemical changes were compensated within 2-6 hrs. in all the group of animals thus increasing the margin of safety.

6) Operations of abdomio-pelvic region of varying duration were successfully performed under these analgesic-anaesthetic combinations making them suitable for use in clinical cases of canines surgical patients.

SUGGESTIONS FOR FURTHER WORKS

1) The cardiopulmonary parameters viz. cardiac index, stroke volume, tidal volume and minute volume of ventilation etc. using propofol alone or in combination with acepromazine or medetomidine may be studied in canines as well as in other species of animals.

2) The acid-base analysis during anaesthesia using these combinations may be studied to, further verify the suitability of these combinations in canines.

3) Reversal studies using alpha $_{2}$- antagonists like atipamezole and yohimbine to reverse the effects of medetomidine-propofol anaesthesia combination may be carried out.

References

REFERENCES

Alexander, F. (1976). Depressants of central nervous system. In: An Introduction to Veterinary Pharmacology 3rd edn., Churchill Livingstone, Edinburg, London. pp 110-111

Alibhai, H.I.K.; Clarke, K.W.; Lee, Y.H. and Thompson, J. (1996). Cardiopulmonary effect of combination of medetomidine hydrochloride and atropine sulphate in dogs. *Vet. Rec.* **136** (1): 11-13.

Baggot, J.D.; Toutain, P.L.; Brandon, R.A. and Alvinerie, M. (1984). Effect of premedication with acetylpromazine on the disposition kinetics of thiopental. *J. Vet. Pharmacology and Therapeutics*, **7**: 197-202.

Batista, C.M.; Laus, J.I.; Nunes, N.; Santos, P.S.P. and Costa, J.L.O. (2000). Evaluation of intraocular and partial CO_2 pressure in dogs anaesthetized with propofol. *Vet. Ophthalmology*. **3** (1): 17-19.

Bayan, H.; Sharma, K.K. and Chakravarty, P. (2002). Biochemical and haematological changes during propofol anaesthesia in canine. *Indian J. Vet. Surgery*, **23** (2): 95 – 96.

Becker, T.; Filho, F.M.; Rocha, K.M.D.; Nascimento, P.R.L.D.; Nascimento, J.A.; Gramio, I.D.F. and Ascoli, F.O. (1998). Comparative study of three doses of atracurium in dogs. (Canis familiaris). *Revista – Brasileira – de – Ciencia – Veterinaria*. **5** (3): 115 – 118.

Berbish, E.A.; Ahmed, K.A. and Mawsouf, M.N. (1998). Effect of ketamine HCl ('Ketalar') R and propofol ('Diprivan') R anaesthesia on blood

coagulation in dogs. A comparative study. *Vet. Med. J. Giza.* **46** (1): 95-104.

Bloor, B.C.; Abdul-Rasool, I.; Temp, J.; Jenkins, S.; Valcke, C.; and Ward, D.S. (1989) The effect of medetomidine, an α_2 – Adrenergic Agonist, on ventilatory drive in the dog. *Actavet. Scand.* 65-70.

Booth, N.H. (1982). Psychotropic agents. In: Veterinary Pharmacology and Therapeutic, 5th edn., IOWA State University Press Ames. pp 321-331.

Bore. (1991) Comparison of endotracheal and intravenous routes of atropine administration in anaesthetized dogs. *Vet. Bull.* **61**. Abst.

Bowman, W.C. (1989) Pharmacology of intravenous anaesthetics and hypnotics in general anaesthesia. Edn. V. Butterworth, London, pp. 115-125.

Brearley, J.C.; Kellaghar, R.E.B. and Hall, L.B. (1988). Propofol anaesthesia in cats. *J. Small Anim. Pract.* 23: 315-322.

Bufalari, A.; Nilsson, L.E.; Shart, C.E.; and Giannoni, C. (1995). A comparative study of neurologically-equivalent propofol anaesthetic combinations in the dog. *J. Vet. Anaesth.* **22:** 19-24.

Bufalari, A.; Short, C.E.; Giannoni, C. and Vaino, O.(1996) Comparative response to propofol anaesthesia alone and with alpha $_2$ adrenergic medications in canine model. *Acta. Vet. Scand.* **37** (2): 187-201.

Bufalari, A.;, Miller, S.M.; Short, C.E. and Giannoni, C. (1997). The use of propofol anaesthesia in dogs premedicated with acepromazine, butorphanol and acepromazine-butorphanol. *Vet. Bull.* **67**. Abst. 8004.

Bufalari, A. (1998a). Plain propofol or propofol associated anaesthesia in dogs: cardiovascular and neurologic effect. *Am. J. Vet. Res.* **79**: 223-227.

Bufalari, A.; Miller, S.M.; Giannoni, C. and Short, C.E. (1998b). The use of propofol as an induction agent for halothane and isoflurane anaesthesia in dogs. *J. Am. Ani. Hosp. Assoc.* **34** (1): 84-91.

Carlson, C. and Champman, A.G. (1981) Clinical and physiological effects of ketamine with or without diazepam or meperidine premedication in dogs. *Anaesthesiol.*, 54: 448.

Claeys, M.A.; Gepts, E. and Camu, F. (1988). Haemodynamic changes during anaesthesia induced and maintained with propofol. *Br. J. Anaes.* **60**: 3-9.

Combrisson, H.; Robin, G. and Cotard, J.P. (1993). Comparative effects of xylazine and propofol on urethral pressure profile of healthy dogs. *Am. J. Vet. Res.* **54** (12): 1986-1989.

Cortopassi, S.R.G.; Holzchun, M.P. and Fantoni, D.T. (2000). General anaesthesia with propofol in dogs premedicated with acepromazine and alfantanil. *Ciencia-Rural*, 30: 4, 635-644.

Cullen, L.K. and Reynoldson, J.A. (1993). Xylazine or medetomidine premedication before propofol anaesthesia. *Vet. Rec.* **132** (15): 378-383.

Cullen, L.K. (1996). Medetomidine sedation in dogs and cats: a review of its pharmacology, antagonism and dose. *Brit. Vet. J.* **152** (5): 519-535.

Cullen, L.K. and Reynoldson, J.A. (1997). Effect of tiletamine/zolazepam premedication on propofol anaesthesia in dogs. *Vet. Rec.* **140**: 363-366.

David, W.P. (1992). Studies on propofol as an intravenous general anaesthetic in dogs. *Indian J Vet. Surgery.* **14** (1): 45.

Davies, C. (1993). Excitatory phenomena following the use of propofol in dogs. *Vet. Bull.* **63**, Abst. 627.

Duke, T. (1995). A new intravenous anaesthetic agent propofol. *Can. Vet. J.* **36** (1): 181-182.

Dundee, J.W. and Wyant, J.M. (1988) Intravenous anaesthesia. Churchill Livngston, pp. 172-182.

England, G.C.; Andrews, F. and Hammond, R.A. (1996). Romifidine as a premedication to propofol induction and infusion anaesthesia in the dog. *Vet. Bull.* **66**. Abst. 4934.

Fantoni, D.T.; Futema, F.; Cortopassi, S.R.G.; Silve L.C.L.C. D.; Verangher, M.; Miranold, R. and Ferreira, M.A. (1999).

Comparative evaluation of acepromazine, detomidine and romifidine in horses. *Vet. Bull.* **69.** Abst. 5583.

Farver, T.B.; Haskins, S.C. and Patz, J.D. (1986). Cardiopulmonary effects of acepromazine and of the subsequent administration of ketamine in the dogs. *Am. J. Vet. Res.* **47**: 631-635.

Fieni, F.; Tainturier, D.; Fau, D.; Genevcis, J.P.; Desmoulins, P.; Bruyas, J.F.; Veillon, A. and Desbois, C. (1990). Application of propofol as a continuous perfusion delivered by electrically operated syringe in dogs. *Vet. Bull.* **61**. Abst. 6076.

Fonda, D. (1991). Continuous infusion anaesthesia with propofol in dogs: Clinically optimized dosages. *J. Vet. Anaes.* (Spl. Supple.) 159-161.

Funkquist, P.; Lofgren, A.M. and Nyman, G. (1993). Propofol-isoflurane anaesthesia for caesarean section in bitches. *Svensk-Veterinartidning.* **45**: 675-680.

Geel, J.K. (1991). The effect of premedication on the induction dose of propofol in dogs and cats. *J. South Afr. Vet. Asso.* **62**: 118-123.

Genevois, J.P.; Fau, D.; Fient, F.; Tainturier, D.; Hosseinzadeh, G.; and Guynnnet, V. (1988). Use of new anaesthetic in the dog: Propofol, Result after injection of a single dose. *Vet.Bull.* **59** Abst. 3688.

Gill, J.R.; Rodriguez, J.F.; Ezauerra, I.J.; Vives, M.A.; Jimenez, J. and Uson, J.M. (1996). Development of anaesthesia and changes in the blood parameters in the dogs medicated with propofol. *Vet. Bull.* **66**. Abst. 8554.

Glen, J.B.; Hunter, S.C.; Bkackbrun, T.P. and Wood, P. (1985). Interaction studies and other investigations of the pharmacology of propofol (Diprivan). Postgrad. Med. J. **61** (Supple): 7-14.

Goodchild, C.S. and Serrao, J.M. (1989). Cardiovascular effects of propofol in the anaesthetized dog. *Br. J. Anaes.* **63**: 87-92.

Grimm, K.A.; Thurmon, J.C.; Tranquilli, W.J.; Benson, G.J. and Greene, S.A. (2001). Anaesthetic and cardiopulmonary effects of propofol in dogs premedicated with atropine, butorphanol and medetomidine. *Veterinary Therapeutics*, **2** (1): 1-9.

Hall, L.W. and Chamber, J.P. (1987). A clinical trial of propofol infusion anaesthesia in dogs. *J. Small Anim. Pract.* **28**: 623-637.

Hall, L.W.; Lagerweij, E.; Nolan, A.M. and Sear, J.W. (1997). Disposition of propofol after medetomidine premedication in Beagle dogs. *J. Vet. Anaes.* **24** (1): 23-29.

Hall, T.L.; Duke, T.; Townsend, H.G.C.; Nigel, A.; Caulkett, N.A. and Cantwell, S.L. (1999). The effects of opoid and acepromazine premedication on the anaesthetic induction dose of propofol in cats. *Can. Vet. J.* **40** (12): 867-870.

Hammond, R.A. and England, G.C.W. (1994). The effect of medetomidine premedication upon propofol induction and infusion anaesthesia in the dog. *J. Vet. Anaesth.* **21** : 24-28.

Heard, J.D.; Webb, A.I. and Daniels, R.T. (1986). Effect of acepromazine on the anaesthetic requirement of halothane in the dog. *Am. J. Vet. Res.* **47**: 2113-2115.

Heldmann, E.; Brown, D.C. and Shofer, F. (1999). The association of propofol usage with postoperative wound infection rate in clean wounds: a retrospective study. *Vet. Surg.* **28** (4): 256-259.

Hellebrekers, L.J.; Herpen, H.V.; Hird, J.F.R.; Rosenhagen C.U.; Sap, R.; Vainio, O. and Van-Harpen, H. (1998). Clinical efficacy and safety of propofol or ketamine anaesthesia in dogs premedicated with medetomidine. *Vet. Rec.* **142** (23), 631-634.

Hellebrekers, L.J. and Sap, R. (1997). Medetomidine as a premedicant for ketamine, propofol or fentanyl anaesthesia in dogs. *Vet. Rec.* **140** (21): 545-548.

Holzchun, M.P., Fantone, D.T. and Cortopassi, S.R.G. (1993). Study of intravenous anaesthesia in dogs with use of propofol effects on arterial pressure and heart rate. *Vet. Bull.* **63**, Abst. 6839.

Hughes, J.M.L. and Nolan, A.M. (1999). Total intravenous anaesthesia in greyhounds: Pharmacokinetics of propofol and fentanyl – a preliminary study. *Vet. Surg.* **28** (6): 513 – 524.

Jain, N.C. (1996). Haematological Techniques. In: Schalm's Veterinary Haematology. 4th Ed. Lee and Febinger, Philadelphia. pp. 20-86.

Jane, E.Q.; Elain, P.R.; Willium, J.R. and Mark, R.F. (1998). Cardiovascular and anaesthetic effects of propofol and thiopentone in dogs. *Am. J. Vet. Res.* **59**: 1137-1143.

Jones, R.S. (1992). Muscle relaxants in canine anaesthesia 2: Clinical application. *J. Small Ani. Pract.* **33**: 423-429.

Keegan, R.D. and Greene, S.A. (1993). Cardiovascular effects of a continuous two hrs propofol infusion in dogs. Comparison with isoflurane anaesthesia. *Vet. Surg.* **22**: 537-543.

Kelawala, N.H. and Parsania, R.R. (1997). Propofol as an intravenous anaesthetic agent in dog. *Ind. Vet. Med. J.* 330 – 332.

Kennis, R.A.; Robertson, S.A.; Rosser, E.J.Jr. and Hauptman, J.G. (1998). Effect of propofol anaesthesia on intradermally injected histamine phosphate in clinically normal dogs. *Am. J. Vet. Res.* **59** (1): 7-9.

Kim, J.W. and Jang, I.H. (1999). The effect of xylazine premedication in the dog. *Korean J. Vet. Clin. Med.* **16** (1): 86-94.

Kim, J.W. and Kim, M.C. (2000). A comparative study on the use of acepromazine/ketamine combination and propofol as an induction agent for influrane anaesthesia in dogs. *Korean J. Vet. Clin. Med.* **17** (2): 395-402.

Komar, E.; Silmanowicz, P. and Balicki, I. (1993). Effect of propofol anaesthesia on gas exchange and haematological parameters in dogs. *Vet. Bull.* **63**, Abst. 4173.

Komar, E. and Bblicki, I. (2000). The effect of atropine, medetomidine, propofol and atipamezol on the hemodynemic parameters of dogs. *Medicina Veterinaria*, **55**, 135-140.

Kramer, S.; Engelke, A. and Nolte, I. (1995). Tonoclonic convulsions after propofol anaesthesia in the dogs. *Kleinterpraxis*. **49**: 30-32.

Kramer, S.; Nolte, I. and Jochle, W.; (1996). Clinical comparison of medetomidine with xylazine/methadone in dogs. *Vet. Rec.* **138** (6) 128-133.

Krik, R.W. (1990). Handbook of Veterinary Procedures and Emergency Treatment. 5th Ed. W.B. Saunders Publisher. Philadelphia. pp 231-251.

Kwon, Y.S.; Jang, K.H.; Kim, J.E.; Chae, H.G.; Lim, J.H.; Lee, K.W. and Jang, I.H. (1999). Effects of continuous administration of propofol in dogs. *Korean J. Vet. Clin. Med.* **16** (2): 363-368.

Langley, M.S. and Heel, R.L. (1988). Propofol: A view of its pharmacodynamic and pharmacokinetic properties and use as an intravenous anaesthetics. *Drugs*. **35**: 334-372.

Lerche, P.; Nolon, A.M. and Reid, J. (2000). Comparative study of propofol or propofol and ketamine for the induction of anaesthesia in dogs. *Vet. Rec.* **146** (20): 571-574.

Light, G.S.; Hardie, E.M.; Young, M.S.; Hellyer, P.W.; Brownie, C. and Hansen, B.D. (1993). Pain and anxiety behaviours of dogs during

intravenous catheterization after premedication with placebo, acepromazine or oxymorphone. *Vet. Bull.* **63**. Abst. 8265.

Lim, J.H.; Jang, K.H. and Jang, I.H. (2000). Comparative effect of propofol infusion rate during maintenance of anaesthesia in dogs *Korean J. Vet. Clin. Med.* **17** (1): 109-120.

Lombard, C.W.; Kvart, C.; Sateri, H.; Holm, G. and Nilsfors, L. (1988). Effects of medetomidine in dogs with mitral regurgitation. *Acta. Vet. Scand.* **85:** 167-174.

Lumb, W.V. and Jones, E.W. (1984) Veterinary Anaesthesia. Lea and Febiger, Philadelphia. pp. 296-299.

Manners, H. (1990). Anaesthesia following medetomidine. *Vet. Rec.* **126** (7): 174.

Miller, C.J.; Mc-Kiernan, B.C.; Pace, J. and Fettman, M.J. (2002). The effects of doxapram hydrochloride (Dopram-V) on laryngeal function in healthy dogs. *J. Vet. Internal Med.* **16** (5): 524-528.

Morgan, D.W.T. and Legge, K. (1989). Clinical evaluation of propofol as an intravenous anaesthetic agent in cats and dogs. *Vet. Rec.* **124**: 31-33.

Muir, W.W. and Gadawski, J.E. (1998). Respiratory depression and apnoea induced by propofol in dogs. *Am. J. Vet. Res.* **59** (2): 157-161.

Murison, P.J. (2001). Effect of propofol at two injection rates or thiopentone on post intubation apnoea in the dog. *J. Small. Anim. Pract.* **42** (2): 71-74.

Najneen, A. (1998). A comparative study of the midline versus the flank approach chlorpromazine hydrochloride versus acepromazine maleate and suture pattern for ovariohysterectomy in canines. M.V.Sc. thesis submitted to K.K.V. Dapoli.

Nakamura, K.; Hatano, Y.; Nishiwada, M.; Toda, H. and Mori, K. (1992). Direct vasoconstrictor and vasodilator effects of propofol in isolated dog arteries. *Br. J. Anaes.* **68** (2): 193-197.

Nilsfors, L.; Gramer, L. and Adolfsson, A. (1989). Sedative and analgesic effects of medetomidine in dogs – an open clinical study. *Acta. Vet. Scand.* **85**, 155-159.

Ozaydin, I.; Atalan, G.; Uzun, M.; Kilic, E. and Cenesiz, M. (2001). Assessment of anaesthetic properties and clinical, cardiovascular and respiratory effects of medetomidine, propofol and ketamine combination in dogs. *Kafkas – Universitesi – Fakultesi – Dergisi,* **7** (1): 71-76.

Patil, A.A.; Sarkate, L.B. and Lokhande, D.U. (1999). Effect of propofol and thiopental sodium as induction agent in canines. In; articles presented in 21st Annual Congress of Indian Society for Veterinary Surgery (ISVS) held at Bhuvaneshwar.

Popovic, N.A.; Mullane. J.F. and Yhap, E.O. (1972). Effect of acetylpromazine maleate of certain cardiopulmonary response in dogs. *Am. J. Vet. Res.* **33**: 1819-1824.

Pugh, D.M. (1964). Acepromazine in veterinary use. *Vet. Rec.* **76**: 439-443.

Quandt, J.E.; Robinson, E.P.; Rivers, W.J. and Raffe, M.R. (1998) Cardiorespiratory and anaesthetic effects of propofol and thiopental in dogs. *Am. J. Vet. Res.* **59** (9): 1137-1143.

Raj, P.A.; Lokhande, D.U.; Sarkate, L.B. and Khandekar, G.S. (2001). In article presented in 23rd Annual Congress of *Indian Society for Veterinary Surgery* (ISVS). held at Channai.

Rand, J.S.; Reynolds, W.T. and Priest, S. (1996). Echocardiographic evaluation of the effects of medetomidine and xylazine in dogs. *Aust. Vet. J.* **73** (2): 41-44.

Raptopopulos, D. and Galatos, A.D. (1997). Gastro-oesophageal reflux during anaesthesia induced with either thiopentone or propofol in the dogs. *J. Vet. Anaes.* **24** (1): 20-22.

Rasmussen, E. (1997). Induction and maintenance of anaesthesia in dogs with Rapinovet and infusion pump. *Dansk – Veterinaertidsskrift*, **80** (23): 991 – 993.

Rauser, P. and Lexmaulova, L. (2002). Clinical comparison of medetomidine-butorphanol and medetomidine-buprenorphine

combinations for intravenous premedication of general anaesthesia in the dog. *Acta – Veterinaria – Brno.* **71** (1): 69-76.

Redondo, J.I., Gomez, R., Sntisteban, J.M., Dominguez, J.M., Galka, M. and Avila, I. (1997). Clinical efficacy of the acepromazine-propofol-halothane and xylazine-propofol-halothane anaesthetic procedures in sick dogs. *Revista – de – Medicina – Veterinaria – Buenos – Aires.* **78** (3): 202-210.

Redondo, J.I.; Gomez, R.; Sntisteban, J.M.; Dominguez, J.M., and Avila, I. (1999). Romifidine, medetomidine or xylazine before propofol-halothane-N_2O anaesthesia in dogs. *Can. J. Vet. Res.* **63** (1): 31-36.

Reid, J., and Nolan, A.M. (1997). Pharmacokinetic of propofol as an induction agent in geriatric dogs. *Vet. Bull.* **67**, Abst. 386.

Rezende, M.L. de.; Farias, A.; Bolzan, A.A.; Ferreira, W.L.; Lega, E.; Nunes, N. and de-Rezende, M.L. (2002). Levomepromazine and acepromazine to blockade the arrhythmia induced by epinephrine in dogs anaesthetized with halothane. *Ciencia-Rural.* **32** (3): 433-438.

Rishniw, M.; Toblas, A.H. and Slinkar, B.K. (1996). Characterization of chronotropic and dysrhythmogenic effects of atropine in dogs and bradycardia. *Vet. Bull.* **66**, Abst. 4915.

Robertson, S.A.; Johnstone, S. and Beemsterbore, J. (1993). Cardiopulmonary anaesthetic and post anaesthetic effects of intravenous infusion of propofol in greyhounds and nongreyhounds. *Vet. Bull.* **63**, Abst 4171

Robin, D.G.; (1987), Tranquilizers and sedatives: In, Principles and Practices of Veterinary Anaesthesia. Ed. by Short, C. E. Williums and Wilkins: **1**, Baltimore, pp-17.

Roush, J.K.; Keene, B.W.; Elcker, S.M. and Bjorling, D.E. (1990). Effect of atropine and glycopyrrolate on oesophageal, gastric and tracheal pH in anaesthetized dogs. *Vet. Bull.* **60**, Abst. 6526.

Salunke, V.M.; Bhokre, A.P.; and Panchbhai, V.S. (2002) Use of propofol in cases of canines. 26th Annual Congress of Indian Society for Veterinary Surgery (ISVS). 21.

Sarkate, L.B.; Lokhande, D.U. and Patil, A.A. (1999). Evalution of propofol as a general anaesthetic in canine surgery – a clinical study. In article presented in 23rd Annual Congress of Indian Society for Vet. Surgery. (ISVS) held at Chennai.

Scabell, P.; Henke, J.; Deppe, H.; Ullrich, M and Erhardt, W. (1999). Comparison of medetomidine drug combination for anaesthesia of dogs. *Tierarztliche – Praxis – Ausgabe – K – Kleintiere – Heimtiere.* **27** (4): 231-238.

Shinkar, D.S. (2002) Studies on the efficacy of detomidine and midazolam as premedicants to propofol anaesthesia in canines. M.V.Sc. Thesis submitted to I.G.K.V.V. Raipur (C.G.)

Short, C.E.; Bufalari, A.; Giannoni, C.; Whitford, K.; Erickson, C. and Tarasoff, S. (1997). A clinical evaluation of pulmonary function in normal and compromised dogs during propofol anaesthesia administration – part 2. *Canine Pract.* **22** (5): 5-14.

Short, C.E.; Gleed, R.D.; Bristol, D.; Meyer, R and Harvey, R. (1982). Antagonistic effects of Dopram-V (doxapram hydrochloride) on xylazine and acepromazine in dogs. *Vet. Med. And Small Anim. Clin.* **77**: 1761-1764.

Smith, J.A.; Gaynor, J.S.; Bednarski, R.M. and Muir, W.W. (1993). Adverse effects of propofol administration with various preanaesthetic regimens in dogs. *J. Am. Vet. Med. Assoc.* **202** (7): 1111-1115.

Snedecor, G.W. and Cocharan, W.G. (1994). Statistical Methods. 8th Ed. East West Press, New Delhi. pp. 254-268.

Steffy, E.P.; Gillespie, J.R.; Berry, J.D.; Eger, E.I. and Schalm, O.W. (1976) Effects of haemocrit and plasma protein concentration in dog and monkey. *Am. J. Vet. Res.* **37**: 959-962.

Stephien R.L.; Bonaghra, J.D.; Bednarski, R.M. and Muir, W.W. (1995). Cardiorespiratory effects of acepromazine maleate and buprenorphine hydrochloride in clinically normal dogs. *Am. J. Vet. Res.* **56**: 78-84.

Sventine, A. and Bjegovi, M. (1995). Comparison of effects of antimuscarinic drugs on spontaneous and stimulated cerebrospinal acetylcholine release. *Vet. Bull.* **65**. Abst. 4910.

Thibaut, J.; Rivera, T. and Ahumada, F. (2002). Intravenous anaesthesia in dogs using a single dose of propofol premedicated with atropine-

acepromazine or atropine-xylazine. (2002). *Archivos – de – Medicina – Veterinaria.* **34** (1): 25-35.

Thurmon, J.C.; Ko, J.C.H.; Benson, G.J.; Tranquilli, W.J. and Olson, W.A. (1994) Haemodynamic and analgesic effects of propofol infusion in medetomidine premedicated dogs. *Am. J. Vet. Res.* **55** (3): 363-367.

Thurmon, J.C.; Tranquilli, W.J. and Ko, J.C.H. (1995). Clinical appraisal of propofol as an anaesthetic in dogs premedicated with medetomidine. *Canine Pact.* **20**: 21-24.

Tiwari, S.K. (1996) Clinicophysiological, cardiopulmonary and heamatobiochemical effects of epidural alpha $_2$ agonist with and without local anaesthetics and their reversal in buffaloes. Ph. D. Thesis submitted to G.B. Pant University of Agriculture and Technology, Pantnagar (Uttaranchal)

Turner, D.M.; Ilkiw, J.E.; Rose, R.J. and Warrem, J.M. (1974). Respiratory and cardiovascular effects of five drugs used as sedative in dogs. *Aus. Vet. J.* **50**: 260-265.

Vaha-Vahe, T. (1989). The clinical efficacy of medetomidine. *Acta. Vet. Scand.* **85**, 151-153.

Vainio, O. (1993). Propofol infusion anaesthesia in dogs premedicated with medetomidine. *Vet. Bull.* **63**, Abst. 626.

Vaisanen, M.; Raekallio, M.; Kuusela, E.; Huttunen, P.; Leppaluoto, J.; Kirves, P and Vainio, O. (2002) Evaluation of the perioperative

stress response in dogs administered medetomidine or acepromazine as part of the preanaesthetic medication. *Am. J. Vet. Res* **63** (7): 969-975.

Viitanen, S.; Heinola, T and Raekallio, M (1998). Propofol infusion anaesthesia after premedication with medetomidine in dogs. *Suomen – elainlaakarilehti.* **104** (6): 331 – 335.

Virtanen, R.; Savola, J.M.; Saano, V. and Nyman, L. (1988). Characterization of the selectivity, specificity and potency of medetomidine as an alpha-$_2$ adrenoceptor, agonist. *Eur. J Pharmacol*, **150**. 9-14.

Virtanen, R. (1989). Pharmacological profiles of medetomidine and its antagonist, atipamezole. *Acta Vet.* **85**, 29-37.

Waechter, R.A. (1982). Unusual reaction to acepromazine maleate in the dog. *J. Am. Vet. Med. Assoc.* **180**: 73-74.

Waterman, A.E. and Hashim, M.A. (1993). Effects of thiopentone and propofol on lower oesophageal sphincter and barrier pressure in dogs. *Vet. Bull.* **63**, Abst. 1992

Watkins, S.B.; Hall, L.W. and Clarke, K.W. (1987). Propofol as an intravenous anaesthetic agent in dogs. *Vet. Rec.* **120**: 326-329.

Watney, G.C.G. and Pablo, L.S. (1992). Median effective dosage of propofol for induction of anaesthesia in dogs. *Am. J. Vet. Res.* **53**: 2320-2322.

Weaver, B.M.Q. and Raptopoulus, D. (1990). Induction of anaesthesia in dogs and cats with propofol. *Vet. Rec.* **126**: 617-620.

Webb, A,I. And O'Brien, J.M. (1988). The effect of acepromazine maleate on the anaesthetic potency of halothane and isoflurane. *Vet. Bull.* **59**: Abst. 2425.

Wooten, T.L. and Lowrie, C.T. (1993). Comparison of cerebrospinal fluid pressure in propofol and thiopental anaesthetized eucapnic dogs. *Vet. Surg.* **22**: 148-150.

Yamashita, K.; Nakashima, M.; Toda, H.; Sasaki, Y.; Tsuzuki, K.; Koike, M., Izumisawa, Y.; Kotani, T. and Muir, W.W. (2001) Medetomidine with thiopental, ketamine or propofol as premedication and induction for inhalation anaesthesia in dogs. *J. Japan Vet. Med. Assoc.* **54** (4): 282-287.

Zoran, D.L.; Riedesel, D.H. and Dyer, D.C. (1993). Pharmacokinetics of propofol in mixed breed dogs and greyhounds. *Am. J. Vet. Res.* **54** (5): 755-760.

"STUDIES ON THE EFFICACY OF ACEPROMAZINE AND MEDETOMIDINE AS PREMEDICANTS TO PROPOFOL ANAESTHESIA IN CANINES"

THESIS ABSTRACT

BY

SANJAY DUBEY

ROLL NO. – 2616 ID. NO. PG/VETY/2001/03

DEPARTMENT OF VETERINARY SURGERY AND RADIOLOGY

COLLEGE OF VETERINARY SCIENCE AND A.H.

INDIRA GANDHI KRISHI VISHWAVIDYALAYA, RAIPUR

ANJORA, DURG (C.G.) - 491001

2003

ABSTRACT

" STUDIES ON THE EFFICACY OF ACEPROMAZINE AND MEDETOMIDINE AS PREMEDICANTS TO PROPOFOL ANAESTHESIA IN CANINES"

By

SANJAY DUBEY

The present study was undertaken to evaluate the efficacy of acepromazine and medetomidine as premedicants to propofol anaesthesia in canines. A total of fifteen mongrel dogs of either sex weighing between 10-15 kg were selected for this study. They were randomly divided into three groups consisting of five dogs each. A pilot study was conducted for standardization of the dose and the minimum effective dose was selected for this study.

The anticholinergic agent atropine sulphate was given to the animals of all the groups @ 0.04mg/kg body weight intramuscularly 15 min prior to start of the treatment. In group I, propofol was administered alone intravenously @ 5 mg/kg body weight. Acepromazine (0.2mg/kg body weight) intramuscularly and medetomidine (20 µg/kg body weight) intramuscularly were administered as preanaesthetic 10 min. prior to propofol anaesthesia in group II and group III respectively.

The clinical parameters viz. onset, duration and complete recovery from anaesthesia, presence or absence of corneal, conjunctival, palpebral, pedal reflexes and relaxation of anal sphincter were monitored. The physiological and cardiopulmonary parameters viz. rectal temperature, heart rate, respiration rate, systolic and diastolic blood pressure and ECG were studied before anaesthesia, 10 min. after premedication and at 5, 15, 30, 60, 90 and 120 min. post anaesthesia. Blood samples were collected before premedication and at 60, 120 and 360 min. after induction of anaesthesia for haematological and biochemical studies.

Induction of anaesthesia was rapid and smooth with propofol. Preanaesthetic administration did not affect the induction time but significantly ($P< 0.01$) increased the duration and complete recovery time from anaesthesia in group II and III. The quality of

analgesia and degree of muscle relaxation was excellent in group III, better in group II and good in group I.

The respiration rate, systolic and diastolic blood pressure showed a significant decrease ($P<0.01$) in group II and III. However, in group I, the changes were less significant ($P<0.05$). The heart rate showed a significant ($P< 0.01$) decrease in all the groups of animals. Rectal temperature showed a non significant decrease in all the groups. Electrocardiogram did not show any significant difference in the duration and amplitude of PQR, ST deflections between group I and II. However in group III, QRS amplitude and T wave showed deflections.

Total erythrocyte count, total leukocyte count, packed cell volume and haemoglobin concentration did not show any significant changes in all the three groups at various time intervals.

Serum glucose and creatinine showed a significant ($P< 0.01$) increase in animals of group II and III while total proteins and SUN values did not differ significantly in all the groups of animals. However, significant increase ($P<0.01$) in AST values was observed in group III animals injected with medetomidine-propofol. The animals of group II also showed a significant ($P< 0.05$) increase at 60 min. post anaesthesia. The ALT values showed a significant ($P< 0.05$) increase at 60 min. post anaesthesia in group II and III animals premedicated with acepromazine and medetomidine before propofol anaesthesia.

Various surgical operations viz. haematoma of ear, castration, spaying, gastrotomy and enterotomy were performed successfully under these preanaesthetic-anaesthetic combinations.

On the basis of this study, it was concluded that medetomidine and propofol combination was safest and produced anaesthesia of longer duration to perform major surgery in canines. Propofol alone and with acepromazine were also safe but their duration of anaesthesia was sufficient to perform short surgical procedures in canines.

Department of Veterinary Surgery & Radiology
College of Veterinary Science & A.H.,
Anjora, Durg (C.G.)
Date: 16/01/04

Signature of
Major Advisor

VITA

The author, Sanjay Dubey was born on 1st July 1965 at Dist. Azamgarh (U.P.). He passed Intermediate examination in the year 1981 from Wesley Inter College, Azamgarh. He passed B. Sc. from Ewing Christian College, Allahabad. He joined College of Veterinary Science and A.H., Jabalpur in the year 1985. After getting B.V.Sc. & A.H. degree, Madhya Pradesh Public Service Commission appointed him as Veterinary Assistant Surgeon in the year 1991. He joined College of Veterinary Science and A. H., Anjora, Durg (Indira Gandhi Agriculture University, Raipur, Chhattisgarh) as an in-service candidate for his Master degree in the Dept. of Veterinary Surgery and Radiology in the year 2002. He completed his course work of M.V.Sc. degree with the O.G.P.A. of 8.73.

Address

Dr. Sanjay Dubey

H.I.G. 166

Padmnabhpur, Durg (C.G.)

491001.