CLINICAL EVALUATION OF XYLAZINE-PROPOFOL ANAESTHESIA IN DOGS

By

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THESIS

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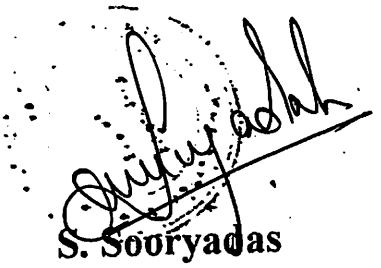
2001

DECLARATION

I hereby declare that this thesis, entitled **"CLINICAL EVALUATION OF XYLAZINE-PROPOFOL ANAESTHESIA IN DOGS"** is a bonafide record of research work done by me during the course of research and that the thesis has not previously formed the basis for the award to me of any degree, diploma, associateship, fellowship or other similar title, of any other University or Society.



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CERTIFICATE

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S. Sooryadas

To
My Friends
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and
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Introduction

INTRODUCTION

The practice of veterinary anaesthesia in the early times consisted primarily of the administration of barbiturates intravenously or diethyl ether by facemask to induce or maintain anaesthesia in small animals. Although good results in terms of anaesthesia were provided, undesirable side effects accompanied these agents. Cardiac and respiratory depression, cumulative effects on repeated administrations, excitable and prolonged recovery phases, perivascular irritation or sloughing, viscid, difficult to inject preparations were the commonly existing problems (Dundee, 1985). But induction and maintenance of anaesthesia with intravenous agents had many potential advantages for a small animal practitioner, especially when acting as surgeon-anaesthetist, because it is easy to manage, nurses can easily be instructed in its use and only comparatively inexpensive apparatus is required.

The problems accompanying the existing anaesthetics led to a continuing need for improving the quality of anaesthesia by introduction of more effective and less toxic drugs and by improving the technique of drug administration. Total intravenous anaesthesia was one such technique, but was accompanied by various side effects. An ultrashort acting anaesthetic, propofol (2,6-diisopropyl phenol), an alkylphenol derivative was found to have desirable anaesthetic profile in animals without much side effects (Glen, 1980). It is available as a one

percent preparation in an aqueous solution of soyabean oil, glycerol, purified egg phosphatide and sodium hydroxide under the trade name of "Propovan".

Propofol is jokingly referred to as the "milk of amnesia" because of its milky white appearance. Propofol is a sedative-hypnotic anaesthetic. It is having rapid onset, ultrashort duration of action, lacks cumulative effects on continuous administration and possesses quick and smooth recovery. The rapid recovery is considered to be a particularly attractive feature in veterinary practice especially in those cases, such as old animals, where the objective is to return the animal to the owner as quickly as possible. But neither sedation nor anaesthesia produced by propofol alone is associated with complete pain relief and muscle relaxation. The use of propofol for maintenance of surgical anaesthesia requires a supplemental analgesic as well as a muscle relaxant. So it is reasonable to assume that a sedative-analgesic-muscle relaxant such as xylazine when combined with hypnotic - propofol would provide useful surgical anaesthesia in dogs with rapid recovery.

Hence, the clinical study was undertaken to evaluate the effects of propofol as an induction as well as maintenance agent for surgical anaesthesia in xylazine premedicated dogs.

Review of Literature

REVIEW OF LITERATURE

Klide *et al.* (1975) compared the effects of intravenous administration of xylazine (1.1 mg/kg) with and without atropine premedication (0.02 mg/kg iv) and intramuscular administration of xylazine (2.2 mg/kg) without atropine premedication in dogs. Xylazine given IV, produced significant decrease in heart rate and aortic flow. Initial increase in blood pressure was followed by decrease, and increase in peripheral resistance. Stroke volume and pulse pressure were not significantly affected. Atropine given IV, did not significantly change any of the effects produced by xylazine. When xylazine was administered im, heart rate and aortic flow decreased significantly, but aortic blood pressure or peripheral resistance was not significantly affected.

Sumano and Fuentes (1979) opined that the use of xylazine as a tranquiliser produced hypotension due to epinephrine liberated by animals under stress.

Adam *et al.* (1980) studied the pharmacokinetics of Cremophor formulation of ICI 35 868 (2,6-diisopropyl phenol, propofol) in rat, pig, rabbit and cat after single intravenous injection. In all species examined, a correlation existed between the systemic blood concentration of propofol and duration of sleep and concentrations in the range of 1-4 μg/ml was effective in producing unconsciousness. No change in pharmacokinetics or in the effective concentration occurred on repeated administration or after infusion.

Glen (1980) evaluated the anaesthetic activity of Cremophor formulation of ICI 35 868 in a range of animal species including rabbits, cats, mice, rats, pigs and monkeys and stated that it is a rapidly acting agent producing anaesthesia of short duration without excitatory side effects. It had similar therapeutic index and produced equivalent cardiovascular and respiratory effects similar to that of thiopentone. In the mouse it was 1.8 times more potent than thiopentone as a hypnotic. However, its anaesthetic profile differed from that of thiopentone in that recovery was rapid following repeated administration. It was also stated that no tissue damage was produced by perivascular or intra-arterial injection.

Peshin *et al.* (1980)observed transient bradycardia and decrease in respiratory rate in dogs following intramuscular administration of xylazine at the rate of 3 mg/kg body weight. Xylazine caused a decrease in T-wave interval and in the amplitude of P-wave and QRS complex. The PR and QT intervals decreased during tachycardia and increased during bradycardia. Changes in the T-wave along with elevation of ST- segment were suggestive of myocardial hypoxia. There was slight decrease in total erythrocyte and leukocyte counts, packed cell volume and haemoglobin concentrations. There was decrease in lymphocyte count with subsequent increase in neutrophil count following xylazine administration. Significant increase in blood glucose, mild increase in serum sodium, and decrease in serum potassium and chloride concentrations were also observed.

Glen and Hunter (1984) compared the effects of aqueous emulsion of propofol containing 10% soyabean oil with that of propofol containing 16% Cremophor in four dogs. Anaesthesia produced with the Cremophor formulation was accompanied by clinical signs of histamine release. Cutaneous hyperaemia was especially noticed 10-15 minutes after induction, defaecation in three of the four dogs and marked salivation and lacrymation in the fourth dog. In animals given the emulsion formulation no untoward effects were noticed.

Hsu *et al.* (1985) reports that an iv injection of 1 mg/kg of xylazine in dogs caused a decrease in heart rate, sinus arrhythmia, and an increase in arterial blood pressure, followed by a decrease. Atropine sulphate (0.045 mg/kg im) increased both arterial blood pressure and heart rate but prevented bradycardia only in 3 out of 5 dogs studied. Other two had to be given a supplemental dose of atropine (0.01 mg/kg iv) before bradycardia was antagonised.

Hall and Chambers (1987) used propofol along with acepromazine (0.05 mg/kg) in atropine (0.02 mg/kg) premedicated dogs. Anaesthesia was induced with propofol 3 mg/kg given as a bolus over 20 seconds and further increments given every 15 seconds until jaw relaxation was adequate for endotracheal intubation. Anaesthesia was maintained with a continuous infusion. It was found that an infusion rate of 0.4 mg/kg/min. of propofol produced surgical anaesthesia. It was concluded that maintenance of anaesthesia was safe with a continuous infusion of propofol.

Watkins *et al.* (1987) evaluated an emulsion formulation of propofol as an intravenous anaesthetic agent in dogs and reported that induction of anaesthesia was smooth and maintenance of anaesthesia was possible by intermittent injection. The mean induction dose in unpremedicated dogs was 5.95 mg/kg. Approximate total dose for maintenance in unpremedicated dogs was 0.806 mg/ kg/min. Premedication with atropine and acepromazine produced a significant reduction in the overall induction dose to 3.81 mg/kg and maintenance dose to 0.373 mg/kg/min. Mean recovery time was 18 min. in unpremedicated dogs given one dose of propofol and in dogs maintained with intermittent injection, mean recovery time was 22 min. from the administration of the last dose. Premedication did not produce statistically significant increase in the recovery times. The quiet, rapid and complete recovery proved to be most valuable in cases where the animal had to be returned to the owners' care with the minimum of delay. Out of 104 premedicated dogs, reduction in respiratory rate was seen in 31 dogs, increase in 44 dogs and there was no change in 29 dogs

Genevois *et al.* (1988) in a trial with 34 unpremedicated dogs observed that propofol given as single intravenous injection at an average dosage of 8 mg/kg effected a very brief period of anaesthesia (an average of 4 min. 42 sec. of analgesia and 7 min. 18 sec before the patient began to raise its head). Dogs could stand and walk normally an average of 14 min. after the injection. Respiratory depression was slight and analgesia and muscle relaxation was sufficient for surgical interventions of short duration.

Bowman (1989) stated that propofol, a weak organic acid with a pKa of 11.0 remains almost entirely unionised at pH 7.4. It gets extensively bound to plasma albumin, leaving a free fraction of only 2% over a wide range of drug concentrations. Propofol gets completely and rapidly metabolised to the sulphate and glucuronic conjugates having no hypnotic properties, and are mainly eliminated by the kidneys.

Brussel *et al.* (1989) studied on the haemodynamic and cardiodynamic effects of induction dose of 2.5 mg/kg propofol in eight dogs. It was observed that propofol was associated with significant decreases in systolic (19.9%) and diastolic (25.3%) arterial pressures associated with a 17.3% decrease in cardiac output (CO) and a 11.6% reduction in systemic vascular resistance (SVR), without change in pulmonary capillary wedge pressure (PCWP). These changes were most pronounced one minute after the injection of propofol. There was a significant decrease in heart rate (HR) at 5 and 10 min. after administration of propofol. It was concluded that in the presence of an unchanged preload, an unchanged HR, and a decreased SVR, the reduction in CO suggests that propofol to have a negative inotropic effect.

Dailland *et al.* (1989) investigated placental transfer and neonatal effects of propofol in 21 women undergoing elective caesarian section under general anaesthesia. In one group anaesthesia was induced with an iv bolus of propofol and maintained with nitrous oxide in oxygen and halothane, and in the other group anaesthesia was induced with propofol and maintained with a continuous

infusion of propofol. It was concluded that in both cases, propofol crossed the placenta but had no apparent major adverse effect on the neonatal outcome parameters.

Goodchild and Serrao (1989) evaluated the cardiovascular effects of propofol in chloralose anaesthetised dogs in combination with iv bretylium and propanolol. It was concluded that anaesthesia with propofol may be accompanied by decreased cardiac output secondary to reduction in preload by a direct venodilator effect. Cardiac output and arterial pressure are preserved well at normal anaesthetic blood concentrations of propofol if the preload was maintained.

Morgan and Legge (1989) observed that the mean induction doses of propofol were 6.55 mg/kg for unpremedicated dogs and 4.50 ± 1.53 mg/kg for dogs premedicated with a tranquiliser. Acepromazine and atropine were the commonest premedicants used although in few cases diazepam, xylazine and other agents were used. Mean recovery time ranged from 23 to 40 minutes. Adverse side effects were infrequent, apnoea during induction being the commonest. No relationship was observed between the number of doses of propofol administered and their recovery times suggesting that it had no cumulative effect when given repeatedly to maintain anaesthesia. In three cases of caesarian section, propofol was used for induction, and maintenance was provided by halothane. The suitability of propofol as an induction agent for this

type of surgery was categorised as good or excellent. Live puppies were delivered in two cases but in the other a single dead puppy was delivered.

Naeije *et al.* (1989) investigated the effects of a continuous infusion (18 mg/kg/h) of the aqueous emulsion formulation of propofol on mean pulmonary arterial/cardiac output and systemic arterial pressure/cardiac output relationships in dogs under pentobarbitone anaesthesia. It was concluded that propofol does not influence pulmonary vascular tone and does not inhibit hypoxic pulmonary vasoconstriction, but reduced systemic vascular tone when venous return or oxygenation was decreased.

Sebel and Lowdon (1989) in the review on propofol as a new intravenous anaesthetic, stated that although the induction dose of propofol decreased arterial pressure, the sympathetic stimulation of intubation reversed this decline, causing a return to preinduction haemodynamic status. In contrast, the arterial pressure of patients treated with thiopental exceeded baseline values after intubation.

Aitkenhead and Smith (1990) reported that during induction of anaesthesia with propofol in healthy young adults, there was delay in disappearance of the eyelash reflex, used normally as a sign of unconsciousness after administration of barbiturate anaesthetic agents. Overdosage of propofol resulted if this clinical sign was used as indicator of depth of anaesthesia. It was also stated that elimination of propofol remained relatively constant even after infusion lasting several days.

Robertson *et al.* (1990) compared propofol infusion anaesthesia in Greyhound and non-Greyhound dogs premedicated with acepromazine and atropine. It was concluded that Greyhound dogs required significantly more propofol (4.0 ± 0.3 mg/kg) for endotracheal intubation than non-Greyhound dogs (3.2 ± 0.1 mg/kg). Propofol was infused at 0.4 mg/kg/min. in all dogs for one hour. Heart rate and respiratory rates were decreased during propofol infusion in Greyhound dogs but not in non-Greyhound dogs. Mean arterial pressure was well maintained in Greyhound dogs but fell in non-Greyhound dogs and was lower than in Greyhound dogs at 25 and 30 minutes. Respiratory acidosis was significant at all times after induction in non-Greyhound dogs but only at 45 and 55 minutes in Greyhound group. Haematocrit was higher and total plasma proteins lowered in Greyhound than non-Greyhound dogs at all times. Recovery was smooth in all dogs. Time to head lift, sternal recumbency and standing was 10.0 ± 1.0, 15.0 ± 3.0 and 28.0 ± 5.0 minutes respectively in non-Greyhound dogs and 36.0 ± 4.0, 43.0 ± 6.0 and 63.0 ± 7.0 minutes in Greyhounds. Propofol produced less cardiopulmonary depression in Greyhounds than in non-Greyhound dogs. Recovery from propofol anaesthesia was slower in Greyhounds than in non-Greyhound dogs.

Weaver and Raptopoulos (1990) reported that the mean induction doses of propofol in unpremedicated and premedicated dogs were 5.2 ± 2.3 mg/kg and 3.6 ± 1.4 mg/kg respectively. The recovery time until the animals were fully recovered, i.e. standing, were 16.4 ± 9.0 min. for unpremedicated dogs and

40.4 ± 26.7 min. for premedicated dogs. One dog showed evidence of pain when propofol was injected. No incompatibility was observed between propofol and the premedicants and the inhalant anaesthetic agents used.

Geel (1991) studied the effect of premedication on the induction dose of propofol in 25 dogs undergoing elective surgical procedures. The induction dose of propofol in dogs younger than 8 years old was 6.9 ± 0.9 mg/kg without premedication and 4.3 ± 1.4 mg/kg with acetylpromazine maleate premedication. The reduction in the induction dose of propofol was statistically significant. When atropine was used together with a fentanyl-droperidol combination or pethidine and acetylpromazine maleate, the mean induction dose was reduced to 2.1 ± 0.1 mg/kg and 2.4 ± 0.3 mg/kg respectively. Propofol was also evaluated as an induction agent in patients undergoing non-elective surgical procedures.

Kamibayashi *et al.* (1991) examined the possible interaction between propofol and epinephrine that might affect the induction of ventricular arrhythmias. It is suggested that propofol enhanced epinephrine-induced arrhythmias in dose-dependent manner in dogs.

Simons *et al.* (1991) observed that after bolus administration, blood concentration of propofol was maximal at 2-15 min., which declined rapidly during the 0-2 hour period and thereafter more slowly. Duration of sleep ranged from 5 - 8 min. Blood concentration of propofol at the end of a six hour infusion also declined at a similar rate to that after the bolus dose. Waking occurred about 44 min. post infusion. It was found that propofol was cleared by conjugation of

the parent molecule or its quinol metabolite. 60-95% of the bolus iv. dose or an infusion dose got eliminated in urine. Biliary excretion leading to enterohepatic circulation occurred.

Cockshott *et al.* (1992) studied the pharmacokinetics of propofol in an emulsion formulation after single bolus and/or multiple infusion to rats, dogs, rabbits and pigs. Protein binding was high (96-98%) and in most species propofol showed appreciable association with the formed elements of blood. It was reported that propofol was distributed into a large initial volume and then extensively redistributed in all species. Clearance of propofol was rapid in all species.

David (1992) evaluated the anaesthetic efficacy of propofol alone and in combination with the preanaesthetic drugs atropine and triflupromazine in 48 non-descript dogs. The mean induction dose required for unpremedicated group was 5.55 mg/kg and for premedicated group 5.02 mg/kg. Induction took about 60 seconds. Males required more induction dose than females. Duration of surgical anaesthesia lasted for four minutes and thirty seconds in unpremedicated and 9 min. in premedicated dogs. Recovery time was 19.5 min. when propofol alone used and 23.27 min. when used in premedicated group. There was significant increase in pulse and heart rate and decrease in respiratory rate and central venous pressure during anaesthesia in both groups. Apnoea of 30–40 seconds were seen during induction. He opined that propofol was an excellent general anaesthetic for dogs.

Nakamura *et al.* (1992) measured the direct effects of propofol on isolated canine cerebral, coronary, mesenteric, femoral and renal arteries and reported that clinically relevant concentrations of propofol did not have direct vasodilator effects.

Watney and Pablo (1992) determined the median effective dose (ED50) of propofol for induction of anaesthesia in 25 dogs premedicated with 0.05 mg/kg acepromazine and in 35 unpremedicated dogs. The ED50 was found to be 2.2 mg/kg in premedicated dogs and 3.8 mg/kg in unpremedicated dogs. Signs of excitement were observed in a few animals of both the groups.

Cullen and Reynoldson (1993) compared the duration of action and cardiopulmonary effects of propofol (6.55 mg/kg iv), xylazine (0.8 mg/kg im) and xylazine plus propofol (3 mg/kg iv) in dogs. Xylazine premedication prolonged propofol anaesthesia in dogs. Propofol alone reduced blood pressure and transiently raised heart rate. Apnoea and hypoxaemia were observed both in premedicated and non-premedicated groups. Bradycardia was a common feature in all dogs given xylazine.

Funquist *et al.* (1993) compared propofol-isoflurane anaesthesia for caesarian section in bitches with that done under epidural or general anaesthesia induced with thiopental. The results were promising, although assistance with initial breathing was sometimes required. Survival rate of puppies was higher after general anaesthesia induced with propofol compared with thiopental. For

puppies considered weak before surgery, the survival rate was higher after epidural anaesthesia.

Keegan and Greene (1993) reported that dogs anaesthetised with propofol (5 mg/kg iv) followed by a propofol infusion beginning at 0.4 mg/kg/min. showed increased value for systemic arterial pressure due to higher systemic vascular resistance. Apnoea and cyanosis were observed during induction. At the end of anaesthesia the mean time to extubation was 13.5 min.. A continuous infusion at the rate of 0.44 mg/kg/min. provided a light plane of anaesthesia.

Komar *et al.* (1993) studied the effect of propofol anaesthesia on gas exchange and haematological parameters in dogs and found that propofol injected in a single dose of 6.5 mg/kg body weight induced general anaesthesia lasting for about 5 minutes. Propofol used continuously at 0.5 mg/kg/min. produced general anaesthesia that was easy to control in depth and time. Continuous infusion caused a transient respiratory acidosis and a decrease of blood oxygenation and a short-lived statistically significant increase in pulmonary shunt.

Pagel and Warltier (1993) opined that the significant decrease in systemic arterial blood pressure observed during continuous propofol anaesthesia in dogs was the result of direct negative inotropic action of propofol along with its direct effects upon arterial and venous vascular tone.

Smith *et al.* (1993) evaluated the effects of propofol with various preanaesthetic regimens in 40 dogs. It was found that intravenous propofol administration induced a variable period of apnoea in 34 dogs. Cyanosis and signs of pain on injection were infrequently observed during induction. Significant decrease in systolic arterial blood pressure was seen both in acepromazine and acepromazine-buterophenol premedicated dogs. It was concluded that propofol when used for induction induced anaesthetic-related adverse effects, which can be minimised by preanaesthetic medication. Recovery characteristics varied with preanaesthetic medication, independent of propofol administration.

Belo *et al.* (1994) stated that even though iv administration of propofol was associated with a considerable decrease in arterial blood pressure. Intracoronary infusion of propofol did not produce any change in systemic arterial blood pressure, heart rate or left ventricular end diastolic pressure. It was suggested that propofol did not have effect on myocardial contractility. The hypotension associated with the intravascular administration of propofol was considered to be due to either a direct vascular or a central effect.

Thurmon *et al.* (1994) evaluated the haemodynamic and analgesic effects of medetomidine (30 μg/kg, im), atropine (0.044 mg/kg, im) and propofol in six healthy adult Beagles. Propofol was administered intravenously (2 mg/kg) as bolus injection for induction, and anaesthesia was maintained with propofol (165μg/kg/min.) for 60 minutes as an intravenous infusion. SA and AV

blockade developed in all the dogs within two minutes of administration of medetomidine and atropine, but disappeared within 10 minutes. Apnoea did not develop after administration of propofol. Analgesia was strong and consistent throughout the entire 60 min. period of infusion. Propofol infusion appeared to alleviate medetomidine-induced vasoconstriction. Recovery was smooth and uncomplicated. Time from termination of propofol infusion to extubation, sternal recumbency, standing and walking unassisted were 29.3 ± 11.9, 61.0 ± 25.4, 79.3 ± 26.6 and 88.2 ± 20.7 min. respectively. The smooth, uncomplicated recovery indicated that continuous infusion of propofol did not have a cumulative effect. It was concluded that the combination was safe for use in healthy Beagles.

Kramer *et al.* (1995) reported the occurrence of tonoclonic convulsions in a four year old Rhodesian Ridgeback bitch and tonic convulsion in a 3 year old Bouvier des Flanders bitch after propofol anaesthesia.

Robinson *et al.* (1995) stated the clinically accepted dose rate of propofol for dogs and cats to be 3 mg/kg iv after xylazine sedation.

Thurmon *et al.* (1995) studied the effects of propofol as an anaesthetic in medetomidine premedicated dogs. It was concluded that propofol, 2 mg/kg iv, 10 minutes after medetomidine (15 or 30 µg/kg) induced satisfactory anaesthesia and endotracheal intubation was easy. Recovery from anaesthesia was rapid and smooth with both drug dose regimens.

Bufalari *et al.* (1996) reported that anaesthetic duration was shorter when propofol was given alone but prolonged when an alpha-2 adrenergic premedicant, medetomidine was combined. Dogs given propofol alone showed a temporary drop in diastolic arterial blood pressure and respiratory frequency, two minutes after induction. Similar respiratory depression was observed in premedicated group also. Apnoea was not observed. An increase in systemic arterial blood pressure was observed throughout the trial in the premedicated group until dogs recovered.

Deryck *et al.* (1996) in the study on systemic vascular effects of isoflurane versus propofol anaesthesia in dogs concluded that compared with isoflurane, propofol preserved aortic pressure better and increased aortic compliance, and thus improved the energy transmission from the left ventricle to the arterial system.

Fodor *et al.* (1996) stated that repeated anaesthesia was possible with propofol, even in geriatric dogs. Patients needed no premedication and maintenance of desired anaesthetic depth was achievable by titrating the propofol dose. The quality of anaesthesia was entirely satisfactory with rapid, quite and complete recovery.

Reid and Nolan (1996) studied the pharmacokinetics of propofol as an induction agent in geriatric dogs and concluded that the induction dose was less and the clearance was slower than that previously reported in young dogs.

Smedile *et al.* (1996) reported excitatory movements during anaesthetic recovery, characterised by forelimb extensor rigidity, opisthotonus, generalised tremor, paddling, horizontal nystagmus and facial twitching in a two-year-old Labrador retriever anaesthetised with iv propofol for bronchoscopy. Excitatory movements persisted for 20 hours.

Funkquist *et al.* (1997) evaluated the use of propofol-isoflurane as an anaesthetic regimen for caesarian section in dogs and compared it with caesarian done under epidural analgesia and caesarian performed under thiopentone anaesthesia. Survival rate of puppies from dams induced with propofol-isoflurane was similar to that for puppies delivered under epidural analgesia. Survival rate for puppies delivered by caesarian section was higher from dams induced with propofol than from dams induced with thiopental sodium.

Redondo *et al.* (1997) compared the clinical efficacy of acepromazine-propofol-halothane and xylazine-propofol-halothane anaesthesia in sick dogs premedicated with atropine. Anaesthesia was induced with propofol iv and maintained by halothane in a mixture of oxygen and nitrous oxide. Mean induction dosage were 3.65 ± 1.24 mg/kg for the xylazine group and 3.39 ± 1.49 mg/kg for the acepromazine group. A higher heart rate and rectal temperature were recorded in the acepromazine group than in the xylazine group. Time to extubation was higher in the xylazine group. There was no significant difference in respiratory rate and the percentage of arterial blood saturation of oxygen.

Bufalari *et al.* (1998) suggested that propofol in combination with inhalant agents, was effective and safe for canine anaesthesia.

Muir 3rd and Gadawski (1998) reported respiratory depression and apnoea as the most likely adverse effects induced by iv administration of propofol to dogs. Propofol administered iv at a rate of 20 mg/kg/10 sec induced minimal cardiovascular depression at dosages in excess of the apnoeic dosage. It was cautioned that respiratory depression and apnoea should be expected as potential adverse effects after iv administration of propofol to dogs, particularly when administered at rapid rates of infusion.

Quandt *et al.* (1998) compared the cardiorespiratory and anaesthetic effects of propofol and reported that anaesthesia was rapid. Respiratory depression and apnoea were major adverse effects associated with propofol and thiopental. Propofol had the advantage of inducing rapid and co-ordinated anaesthesia. Time to sternal position and walking unaided were significantly shorter with propofol.

Kim *et al.*(1999) reported that loss of toe-web needle prick response, duration of anaesthesia and recovery time were dependent on dose of premedicant–xylazine in dogs anaesthetised with propofol. Body temperature decreased gradually after administration of anaesthetics in both cases. Heart rate significantly decreased after propofol injection. There was no significant change in total leukocyte and total erythrocyte counts. Significant increase in total protein and albumin values were noticed after anaesthesia in dogs premedicated

with 2 mg/kg xylazine. It was suggested that premedication with xylazine can help to decrease dosage of propofol and incidence of side effects and recommended administration of xylazine at the rate of 1 mg/kg as pre-anaesthetic before propofol anaesthesia in the dog.

Materials and Methods

MATERIALS AND METHODS

The study was carried out in fifteen dogs of different breeds of either sex, presented to the clinics of the college for various surgical interventions. These animals were divided into two groups viz. group I and group II.

Group I – consisted of eight apparently healthy dogs presented for elective surgery (Table-1) and were serially numbered as A1 to A8.

Group II– consisted of seven diseased dogs which required emergency surgical treatment (Table-2) and were serially numbered from B1 to B7.

Preoperative considerations

All the animals were clinically examined pre-operatively and radiographs were taken when needed to supplement the diagnosis.

Preparation of the patient

Dogs of group I were kept off feed for 12 hours before anaesthesia. Fluid deficit of animals in group II was corrected by administration of Ringer lactate prior to anaesthesia. The site of operation was prepared in the routine manner as for aseptic surgery.

Anaesthesia

Pre-anaesthetic medication

All the animals were premedicated with atropine sulphate[1] @ 0.04 mg/kg body weight intramuscular (im) immediately followed by xylazine[2] @ 1.0 mg/kg body weight (im).

General anaesthesia

Ten minutes after administration of the pre-anaesthetic medication, general anaesthesia was induced by intravenous administration of one percent solution of propofol[3] (Fig.1) 'to effect'.

Induction of anaesthesia

Induction of surgical anaesthesia was assessed by noting the disappearance of jaw muscle tone and relaxation of laryngeal muscles which allowed endotracheal intubation.

Maintenance of anaesthesia

Anaesthesia was maintained by incremental dose(s) of propofol as bolus injection(s).

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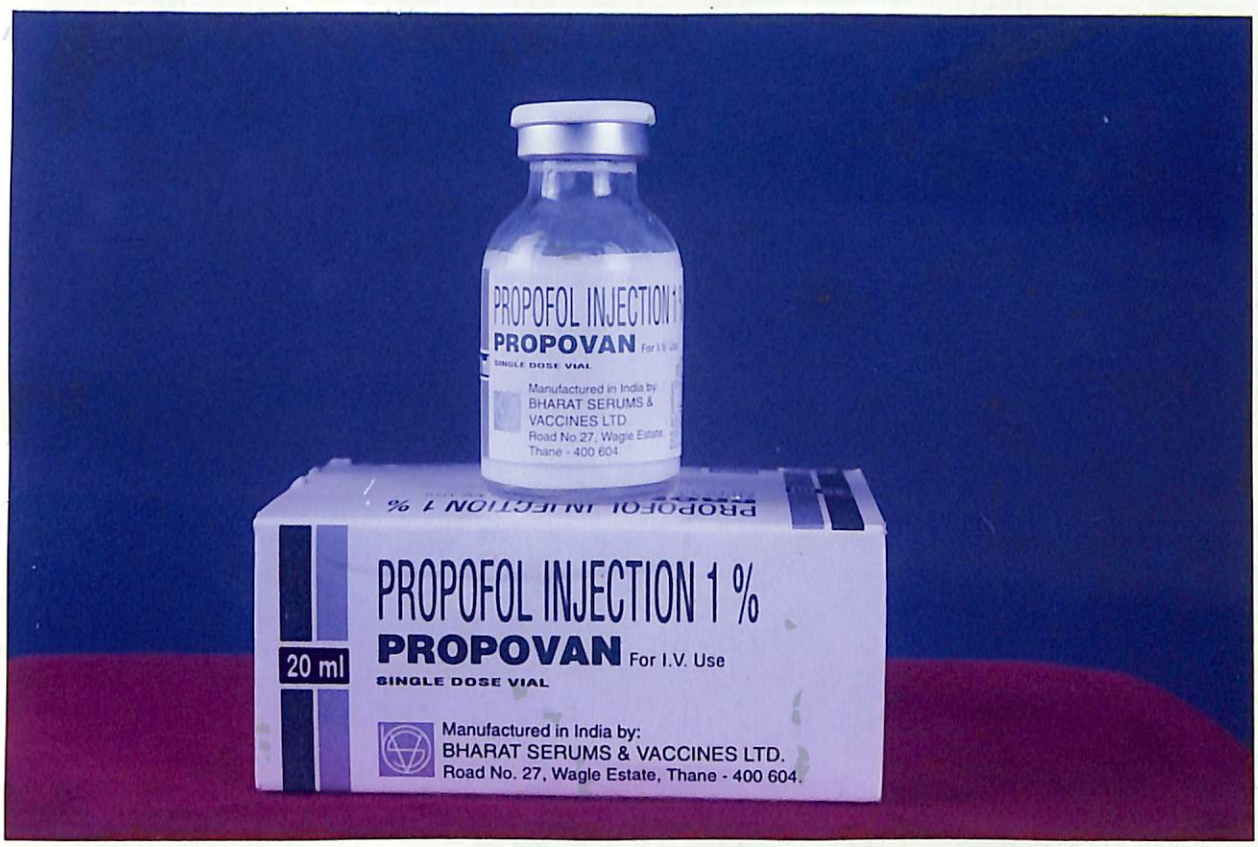
1. ATROWOK™ - Wockhardt Limited, Nani Daman, Mumbai
2. XYLOCAD - Cadila Pharmaceuticals Ltd., Ahmedabad
3. PROPOVAN (Propofol injection 1%) - Bharat Serums and Vaccines Ltd., Thane


PROPOFOL INJECTION 1 %
PROPOVAN For I.V. Use
SINGLE DOSE VIAL
Manufactured in India by:
BHARAT SERUMS & VACCINES LTD.
Road No. 27, Wagle Estate, Thane - 400 604.
20 ml

Main items of observations

Anaesthetic parameters

1. Clinical signs

The various clinical signs observed after preanaesthetic medication, during induction and maintenance, and on recovery were recorded.

2. Induction dose

It was calculated as the quantity(in milligrams)of propofol required per kilogram body weight for induction of general anaesthesia.

3. Induction time

It was calculated as the time from initiation of injection of propofol to the time of disappearance of jaw muscle tone and relaxation of laryngeal muscles, which allowed endotracheal intubation.

4. Duration of anaesthesia after induction bolus

Duration of anaesthesia was calculated as the time from induction to the first incremental bolus.

5. Average incremental dose

Average incremental dose was calculated by dividing the sum total of propofol given as increment doses with the total number of increments given and again dividing with the body weight of the animal.

6. Average duration of effect of incremental bolus

Average duration of effect of incremental bolus was calculated by dividing the sum total duration obtained by the incremental boluses with the total number of increments given for maintenance.

7. Rejection of endotracheal tube (recovery)

The time from administration of last bolus to the time of rejection of endotracheal tube was recorded.

8. Recovery parameters

The time from recovery to head lifting, resuming of sternal recumbency, standing and walking with apparently normal gait were also recorded.

Physiological observations

1. Respiration rate (per min.) was recorded before and after premedication and every 15 min. after induction with propofol till recovery.

2. Pulse rate (per min.) was recorded before and after premedication and every 15 min. after induction with propofol till recovery.

3. Rectal temperature (^{0}C) was recorded before and after premedication and every 15 min. after induction with propofol till recovery.

4. Electrocardiogram (ECG) was recorded before and after premedication and every 15 min. after induction with propofol till recovery.

It was recorded using lead II system using Cardiart - 108 T[1], at a paper speed of 25 mm per second.

5. Systolic, diastolic and **mean arterial blood pressures** (mm Hg) were recorded before and after premedication, and every 15 min. after induction of anaesthesia till recovery.

An inflatable paediatric cuff was fixed on to the forelimb above the point of elbow and inflated. An acoustic stethoscope was placed below the cuff on the medial aspect of the limb on the radial artery. Both the systolic and diastolic sounds were auscultated and recorded using a sphygmomanometer, calibrated in millimetres of mercury (Harvey *et al.*, 1983).

Collection of blood samples

From all the animals, blood samples were collected from the cephalic vein, before and after premedication and at every 20 minutes after induction with propofol till recovery and on the 7th postoperative day, for evaluation given hereunder.

(a) Haemogram

Erythrocyte sedimentation rate (ESR) (Wintrobe, 1961), packed cell volume (PCV) (Wintrobe, 1961), haemoglobin concentration, and

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1. CARDIART – 108 T, BPL India

erythrocyte (RBC), total leukocyte (TLC), neutrophil, lymphocyte, eosinophil, monocyte and basophil counts were recorded (Schalm, 1975).

(b) Serum constituents

Serum sodium and **potassium** concentrations were estimated before and after premedication and every 20 min. after induction till recovery by flame photometric method.

Total serum protein and **Albumin/Globulin ratio** were estimated before and after premedication and on the 7^{th} postoperative day using protein and albumin kit[1] by Biuret and BCG dye binding method.

Statistical analysis

Since the duration of operation varied for each animal in both groups, the physiological and haematological parameters upto 15 min. and serological parameter upto 20 min. could only be statistically analysed. Within group comparison of the data was carried out using Paired t-Test and between group comparison using Students t-Test (Snedecor and Cochran, 1967).

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1. TOTAL PROTEIN AND ALBUMIN KIT – Dr. Reddy's Laboratories, Hyderabad

Table 1. Breed, sex, age, body weight and the surgical condition in Group I animals

No.	Breed	Sex	Age	Body weight (kg)	Surgery/condition
A1	Boxer	Female	3 months	6	Cropping
A2	Great Dane cross	Female	2 years	24	Spaying
A3	Mongrel	Female	1 year	10	Spaying
A4	Spitz	Male	6 years	6	Haematoma auris
A5	Great Dane cross	Female (spayed)	2½ years	26	Haematoma auris
A6	Dobermann pinscher	Male	3 months	10	Docking
A7	German Shepherd	Male	2 years	27	Haematoma auris
A8	German Shepherd	Male	6 years	25	Haematoma auris

TABLE 2. Breed, sex, age, body weight and the surgical condition in Group II animals.

No.	Breed	Sex	Age	Body weight (kg)	Surgery/ Condition
B1	Dobermann pinscher	Male	6 months	10	Ileo-colic intussusception
B2	Rottweiler	Female	3½ years	25	Gastro-splenic torsion
B3	Spitz	Female	4 years	7	Tibial fracture
B4	Dobermann pinscher	Male	6 months	13	Pelvic and femur fracture
B5	Boxer	Male	5 years	20	Caeco-colic obstruction
B6	Dachshund	Female	2 years	10	Caesarian
B7	Dachshund	Female	8 years	9	Mammary tumour and Ventral abdominal hernia

Results

RESULTS

GROUP I

This group comprised of eight dogs, presented for planned operations (Table-1). The observations are presented in Tables 3-7.

Observations during Anaesthesia

1. Response after premedication

Administration of xylazine brought about sedation in animals manifested by winking of eyes and incoordination of movements with lowering of head and neck. Attempts to vomit was noticed in three animals.

The animals assumed sternal recumbency by 3.28 ± 0.17 minutes and lateral recumbency by 5.89 ± 0.15 minutes after administration of xylazine and atropine.

2. Response after propofol administration

Breath holding for 15 seconds was observed during induction of general anaesthesia with propofol in A3, A6 and A7.

Palpebral reflex was sluggish in all animals except A2 where the palpebral reflex abolished during induction and later reappeared and was sluggish throughout period of maintenance.

Eyeball rolled down during induction and remained in that position throughout the anaesthetic period in all animals except one dog (A2), in which the eyeball rolled down and returned to central position.

The jaw muscles were relaxed and permitted endotracheal intubation in all the dogs. Pedal reflex disappeared in all the animals. Relaxation of abdominal muscles and limbs was good in all the animals. Anal sphincter relaxation was observed throughout the period of maintenance in two animals (A2 and A5).

Urination during induction of anaesthesia was observed in two animals (A2 and A5), after resuming sternal recumbency in one dog (A3), and after standing up in one dog (A7). Dribbling of urine was noticed throughout the period of anaesthesia in two dogs (A2 and A5). Defecation was noticed during the period of maintenance of anaesthesia in one dog (A3).

Seizure like movements were noticed during recovery in three animals - forelimb stiffness along with shivering (A2), stiffness of neck and extension of head (A3) and paddling of fore limbs (A7).

Smacking was observed in one animal (A2) after rejection of endotracheal tube.

3. Induction dose and time

Induction dose of propofol was 5.09 ± 0.59 mg/kg and induction time was 4.20 ± 1.08 minutes.

4. Duration of anaesthesia after induction dose

Duration of anaesthesia after induction dose was 14.03 ± 2.04 minutes.

5. Average incremental dose and duration of effect

Average incremental dose needed for maintenance of anaesthesia was 2.78 ± 0.45 mg/kg body weight.

Average duration of effect of incremental bolus was 10.04 ± 0.75 minutes.

6. Rejection of endotracheal tube

Animals rejected the endotracheal tube by 12.56 ± 1.57 min after last incremental bolus.

Lifting of head after recovery took 2.41 ± 0.58 min. Animals resumed sternal recumbency by 7.94 ± 1.42 min and was able to stand by 14.72 ± 1.63 min after recovery. The gait of the animal became apparently normal by 19.69 ± 1.55 minutes.

Physiological observations

Respiration rate (per minute) was 50.5 ± 9.65 and 24.25 ± 5.22 before and after premedication respectively and 17.13 ± 2.88 at 15 min after induction with propofol. There was decrease in respiration rate after premedication and at

15 min after induction with propofol. The decrease was significant ($p<0.01$) after premedication and at 15 min after induction of anaesthesia with propofol.

Pulse rate (per minute) was 106.75 ± 4.72 and 103.5 ± 15.8 before and after premedication respectively and 125.5 ± 8.64 at 15 min after induction. There was decrease in pulse rate after premedication and increase in pulse rate at 15 min after induction. The increase was significant at 15 min ($p<0.05$).

Rectal temperature (^{0}C) was 39.31 ± 0.18 and 39.41 ± 0.23 before and after premedication respectively and 38.99 ± 0.22 at 15 min after induction. There was a significant decrease ($p<0.01$) in the temperature at 15 min after induction compared to that after premedication.

Heart rate (per/min.) was 140.38 ± 8.61 and 132.0 ± 20.96 before and after premedication and 161.0 ± 10.75 at 15 min. after induction. The heart rate was higher at 15 min., though not significant.

Electrocardiogram

After premedication

Heart rate – Tachycardia was observed in three animals (A1, A3 and A8) after premedication. Marked decrease in heart rate with 2nd degree heart block was noticed in dogs A4 and A5 (Fig.2A).

P wave – Changes in the height of P wave (wandering pacemaker) was noticed in animals A3 and A8. P wave sometimes overlapped QRS (ventricular

pre-excitation) in animal A3 (Fig.2B). P on T wave (Atrial premature contraction) was noticed in animal A4 (Fig.2A).

ST segment – ST coving was observed in one dog (A3) after premedication (Fig.2B).

After induction

Heart rate : 15 min. post induction the heart rate increased from the post premedication value in all the animals except one (A8). Tachycardia was seen in three animals (A1, A3 and A6) (Fig.3A).

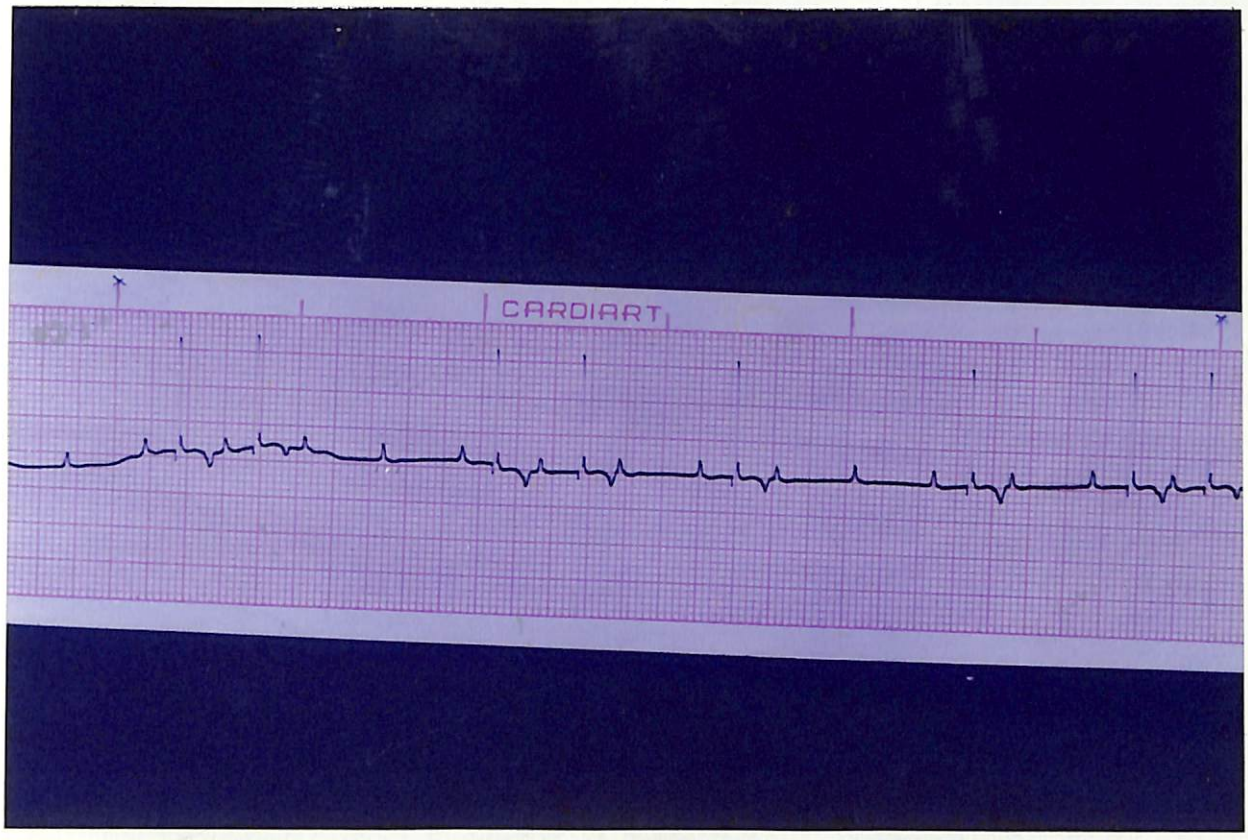
T wave – T wave was biphasic (Fig.3B) at 45 min. and negative and more than ¼ R wave at 60 min. and 75 min. after induction in one dog (A3).

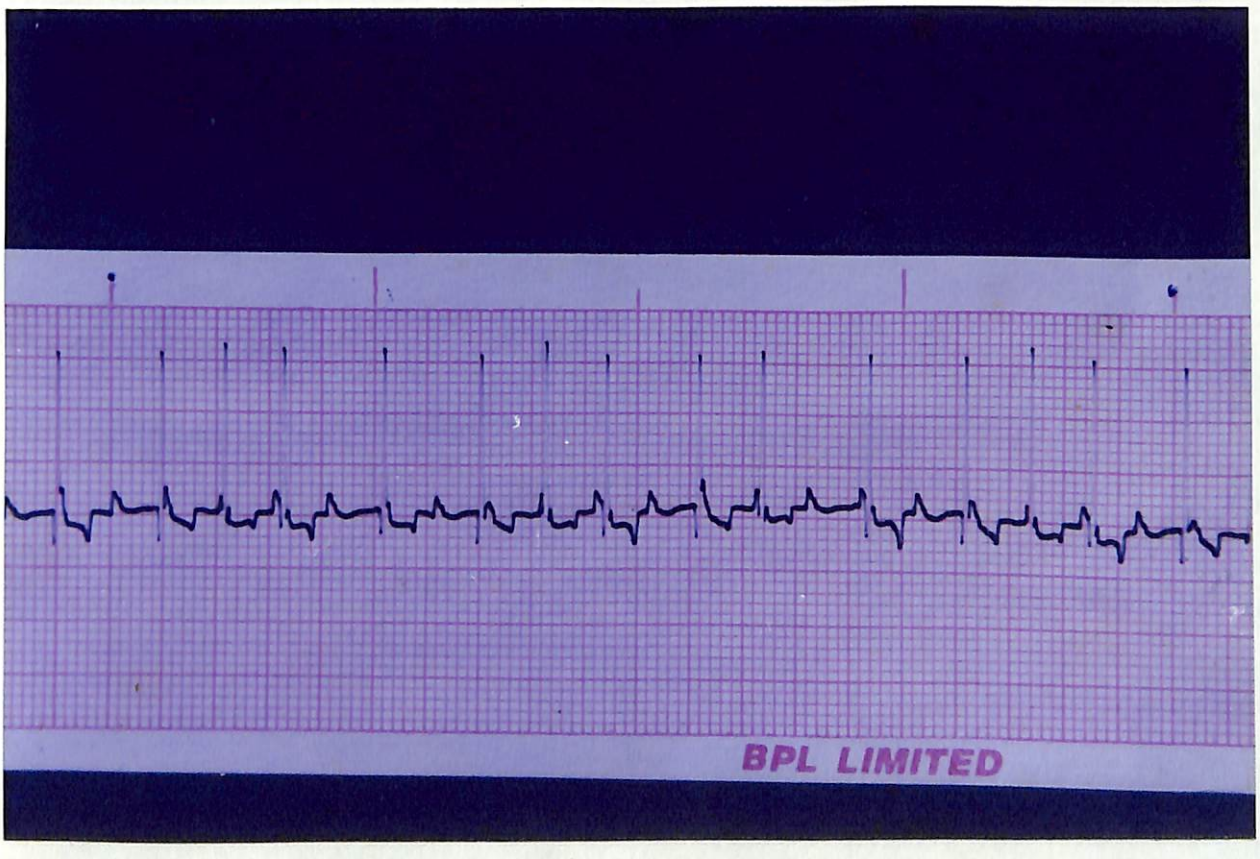
Systolic blood pressure

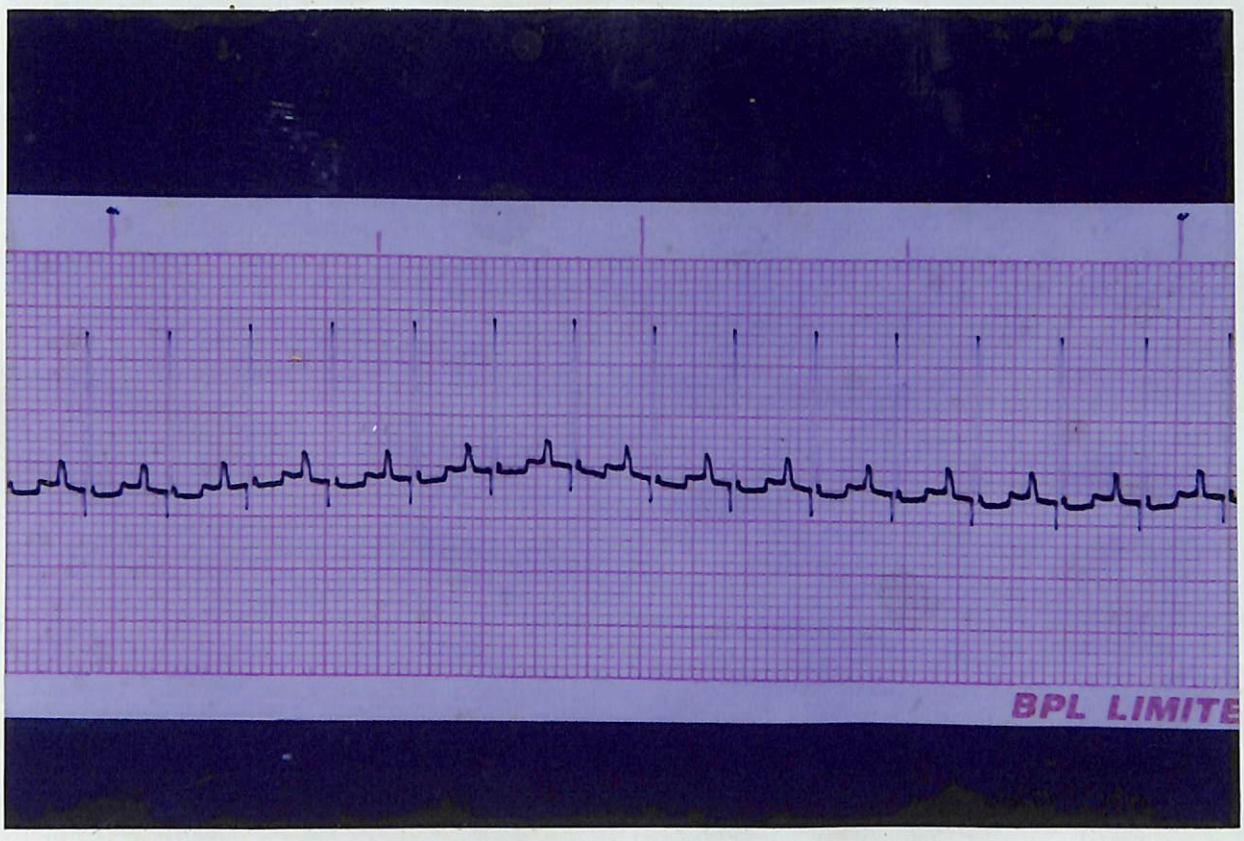
Systolic blood pressure (mm Hg) was 169.75 ± 7.77 and 135.5 ± 8.17 before and after premedication respectively and 210.25 ± 11.31 at 15 min. after induction. There was significant decrease ($p<0.01$) in systolic blood pressure after premedication with xylazine and increase ($p<0.05$) at 15 min. after induction with propofol. The increase at 15 min post induction was highly significant ($p<0.01$) compared to the value after premedication.

Diastolic blood pressure

Diastolic blood pressure (mm Hg) was 128.5 ± 5.34 and 99.63 ± 8.14 before and after premedication respectively and 176.75 ± 10.75 at 15 min. after


CARDIART


BPL LIMITED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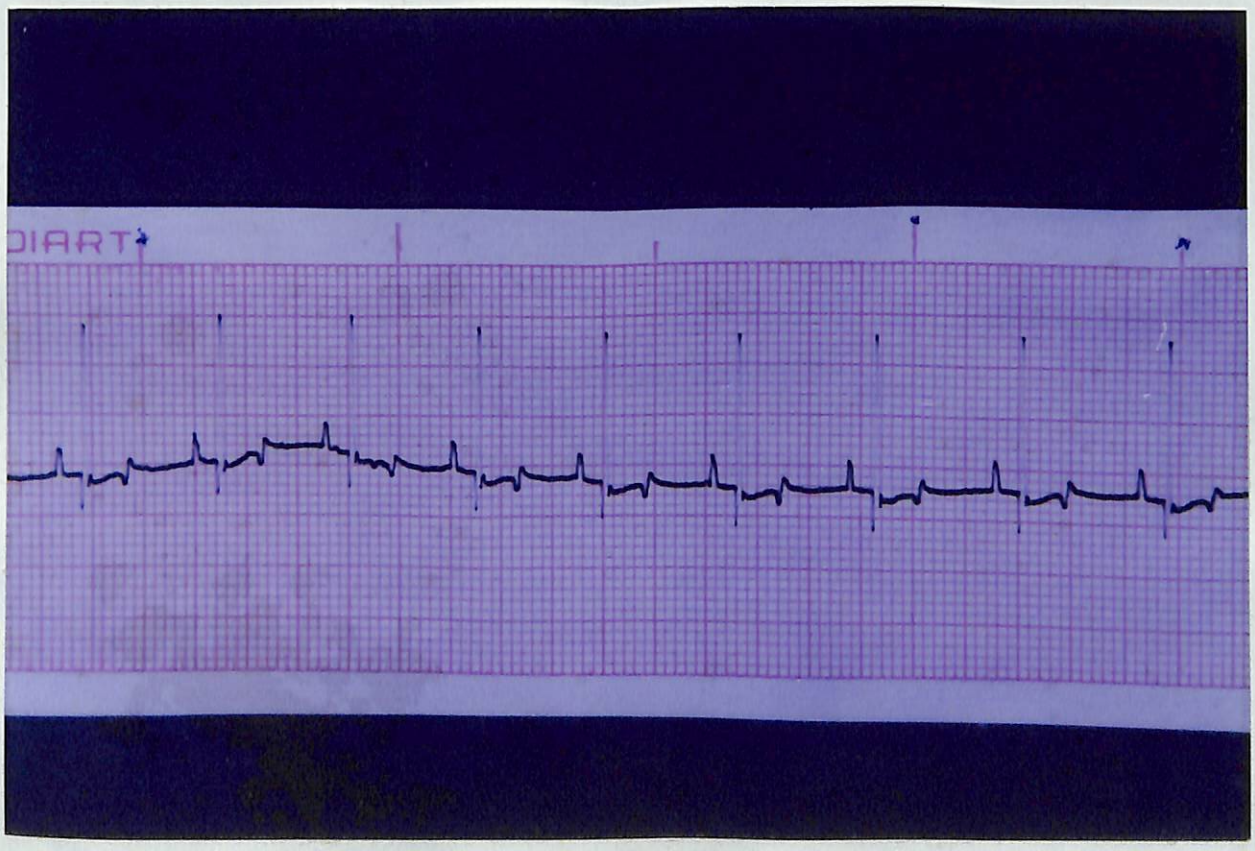
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induction. The decrease after premedication was significant ($p<0.05$). The increase at 15 min after propofol was highly significant ($p<0.01$) compared to the value before and after premedication.

Mean arterial blood pressure

Mean arterial pressure (mm Hg) was 149.13 ± 6.39 and 117.56 ± 8.03 before and after premedication respectively and 193.5 ± 10.85 at 15 min after induction with propofol. There was a highly significant decrease in mean arterial blood pressure after premedication ($p<0.01$) and a significant increase after induction with propofol ($p<0.05$). The increase after induction was highly significant ($p<0.01$) when compared to the post premedication value.

Haemogram

Erythrocyte sedimentation rate (mm/30 min) was 1.89 ± 0.13 and 1.5 ± 0.19 before and after premedication and 1.31 ± 0.13 at 20 min after induction with propofol. The changes observed were marginal and within normal range.

Packed cell volume (per cent) was 35.13 ± 2.33 and 31.13 ± 1.80 before and after premedication and 33.5 ± 1.96 at 20 min after induction with propofol. The decrease seen after premedication was significant ($p<0.05$). The increase seen 20 min. post induction was highly significant compared to the value after premedication.

Haemoglobin concentration (g/dl) was 9.34 ± 0.76 and 8.54 ± 0.53 before and after premedication and 9.05 ± 0.66 at 20 min after induction with propofol. The changes were marginal and within normal range. There was a significant increase in haemoglobin at 20 min. post induction from the after premedication value.

Erythrocyte count (x $10^6/mm^3$) was 5.5 ± 0.21 and 4.81 ± 0.24 before and after premedication and 5.25 ± 0.28 at 20 min after induction with propofol. There was significant decrease in the count after premedication ($p<0.01$). The increase at 20 min. post induction was highly significant.

Total leukocyte count (x $10^3/mm^3$) was 9.68 ± 0.85 and 8.4 ± 0.59 before and after premedication and 9.82 ± 0.56 at 20 min after induction with propofol. The decrease seen after premedication was significant ($p<0.01$). The increase at 20 min. post induction was highly significant.

Neutrophil count (per cent) was 60.28 ± 1.6 and 67.83 ± 2.53 before and after premedication and 67.14 ± 2.28 at 20 minutes after induction with propofol. The increase was significant in both after premedication and at 20 min after induction ($p<0.01$).

Lymphocyte count (per cent) was 37.44 ± 1.39 and 30.94 ± 2.60 before and after premedication and 31.93 ± 2.55 at 20 min after induction with propofol. The decrease after premedication and at 20 min after induction was significant.

Monocyte count (per cent) was 0.79 ± 0.29 and 0.43 ± 0.23 before and after premedication and 0.40 ± 0.34 at 20 min after induction with propofol. There was a gradual decrease in count, but the variation was within normal range.

Eosinophil count (per cent) was 1.26 ± 0.57 and 0.71 ± 0.35 before and after premedication and 0.34 ± 0.19 at 20 min after induction with propofol. The decrease seen after premedication was significant ($p<0.05$).

The changes in basophil count (per cent) were not significant.

Serum constituents

Serum sodium concentration (mEq/l) was 72.43 ± 1.07 and 72.55 ± 1.64 before and after premedication and 72.83 ± 0.81 at 20 min after induction with propofol. The changes observed were marginal and within normal range.

Serum potassium concentration (mEq/l) was 2.53 ± 0.19 and 2.76 ± 0.19 before and after premedication and 2.75 ± 0.12 at 20 min after induction with propofol. A gradual increase within normal range was observed after premedication and after induction with propofol. Total serum protein (g/dl) was 7.25 ± 0.25 and 7.88 ± 0.44 before and after premedication and 7.5 ± 0.27 on the seventh postoperative day. There was slight increase within normal range after premedication and at 7^{th} day.

Albumin/Globulin (A/G) ratio was 0.66 ± 0.06 and 0.60 ± 0.08 before and after premedication and 0.71 ± 0.07 on the seventh postoperative day. The changes were marginal and within normal range.

Table-3. Induction time, duration of anaesthesia and time of recovery after xylazine-atropine premedication and propofol anaesthesia in Group I animals (n=8)

Assumption of sternal recumbency after preanaesthetic medication (min.)	3.28 ± 0.17
Assumption of lateral recumbency after preanaesthetic medication (min.)	5.89 ± 0.15
Induction dose (mg/kg) of propofol administered	5.09 ± 0.59
Induction time (min.)	4.20 ± 1.08
Duration of anaesthesia after initial bolus (min.)	14.03 ± 2.04
Average incremental dose of propofol (mg/kg) administered	2.78 ± 0.45
Average duration of anaesthetic effect of incremental dose (min.)	10.04 ± 0.75
Rejection of endotracheal tube after last bolus (min.)	12.56 ± 1.57
Head lifting after recovery (min.)	2.41 ± 0.58
Assumption of sternal recumbency after recovery (min.)	7.94 ± 1.42
Standing after recovery (min.)	14.72 ± 1.63
Walking after recovery (min.)	19.69 ± 1.55

Table-4. Effect of administration of propofol with xylazine-atropine premedication on respiration rate, pulse rate, temperature and heart rate in Group I animals (Mean ± SE) (n=8)

Parameter	Before premedication	After premedication with xylazine and atropine	15 minutes after induction with propofol
Respiration (per/min)	50.5 ± 9.65	24.25 ± 5.22**	17.13 ± 2.88**
Pulse (per/min)	106.75 ± 4.72	103.5 ± 15.80	125.5 ± 8.64*
Temperature (^{0} C)	39.31 ± 0.18	39.41 ± 0.23	38.99 ± 0.22^{aa}
Heart rate (per/min)	140.38 ± 8.61	132.0 ± 20.96	161.0 ± 10.75

* - Significant at 5% level as compared to value before premedication($P<0.05$)

** - Significant at 1% level as compared to value before premedication($P<0.01$)

aa - Significant at 1% level as compared to value after premedication($P<0.05$)

Table-5. Effect of administration of propofol with xylazine-atropine premedication on systolic, diastolic and mean arterial blood pressures in Group I animals (Mean ± SE) (n=8)

Parameter	Before premedication	After premedication with xylazine and atropine	15 minutes after induction with propofol
Systolic blood pressure (mm Hg)	169.75 ± 7.77	135.5 ± 8.17**	210.25 ± 11.31* aa
Diastolic blood pressure (mm Hg)	128.5 ± 5.34	99.63 ± 8.14*	176.75 ± 10.75** aa
Mean blood pressure (mm Hg)	149.13 ± 6.39	117.56 ± 8.03**	193.5 ± 10.85* aa

* - Significant at 5% level as compared to value before premedication($P<0.05$)

** - Significant at 1% level as compared to value before premedication($P<0.01$)

aa - Significant at 1% level as compared to value after premedication($P<0.05$)

Table-6. Effect of administration of propofol with xylazine-atropine premedication on haematological parameters in Group I animals (Mean ± SE) (n=8).

Parameter	Before premedication	After premedication with xylazine and atropine	20 minutes after induction with propofol
ESR (mm/30 min)	1.89 ± 0.13	1.5 ± 0.19	1.31 ± 0.13
PCV (per cent)	35.13 ± 2.33	31.13 ± 1.80*	33.5 ± 1.96^{aa}
Haemoglobin (g/dl)	9.34 ± 0.76	8.54 ± 0.53	9.05 ± 0.66^{a}
RBC (x 10^6/mm^3)	5.5 ± 0.21	4.81 ± 0.24**	5.25 ± 0.28^{aa}
TLC (x10^3/mm^3)	9.68 ± 0.85	8.4 ± 0.59**	9.82 ± 0.56^{aa}
Neutrophil (per cent)	60.28 ± 1.6	67.83 ± 2.53**	67.14 ± 2.28**
Lymphocyte (per cent)	37.44 ± 1.39	30.94 ± 2.60**	31.93 ± 2.55*
Monocyte (per cent)	0.79 ± 0.29	0.43 ± 0.23	0.40 ± 0.34
Eosinophil (per cent)	1.26 ± 0.57	0.71 ± 0.35*	0.34 ± 0.19
Basophil (per cent)	0.24 ± 0.22	0.10 ± 0.09	0.20 ± 0.13

* - Significant at 5% level as compared to value before premedication($P<0.05$)

** - Significant at 1% level as compared to value before premedication($P<0.01$)

a - Significant at 5% level as compared to value after premedication($P<0.05$)

aa - Significant at 1% level as compared to value after premedication($P<0.05$)

Table-7. Effect of administration of propofol with xylazine-atropine premedication on the serum biochemical parameters in Group I animals (Mean ± SE) (n=8).

Parameter	Before premedication	After premedication with xylazine and atropine	20 minutes after induction with propofol	Seventh day
Sodium (mEq/l)	72.43 ± 1.07	72.55 ± 1.64	72.83 ± 0.81	--
Potassium (mEq/l)	2.53 ± 0.19	2.76 ± 0.19	2.75 ± 0.12	--
Total protein (g/dl)	7.25 ± 0.25	7.88 ± 0.44	--	7.5 ± 0.27
A/G Ratio	0.66 ± 0.06	0.60 ± 0.08	--	0.71 ± 0.07

Table-8. Signs observed during induction, maintenance and recovery in Group I animals (n=8)

	Breath holding during induction	Palpebral reflex	Status of eyeball	Pedal reflex	Relaxation of jaw muscles	Relaxation of abdominal muscles	Relaxation of anal sphincter	Urination	Defecation	Seizure like movements
A1	-	+	X	Abolished	Good	Good	--	--	--	--
A2	-	++	XX	Abolished	Good	Good	**	#	--	@
A3	For 15 seconds	+	X	Abolished	Good	Good	--	##	$	@@
A4	-	+	X	Abolished	Good	Good	--	--	--	--
A5	-	+	X	Abolished	Good	Good	**	#	--	--
A6	For 15 seconds	+	X	Abolished	Good	Good	--	--	--	--
A7	For 15 seconds	+	X	Abolished	Good	Good	--	###	--	@@@
A8	-	+	X	Abolished	Good	Good	--	--	--	--

\+ - Sluggish throughout anaesthetic period
++ - Abolished on induction and reappeared after induction and sluggish throughout maintenance
X - Rolled down during induction and remained in that position throughout the anaesthetic period
XX - Rolled down and returned to centre on induction
** - Relaxed on induction and remained open throughout anaesthetic period
\# - Dribbling of urine throughout maintenance of anaesthesia
- Urinated after resuming sternal recumbency
- Urinated after standing up
$ - Defecated during maintenance period
@ - Stiffness of forelimbs along with shivering during recovery
@@ - Shivering after last incremental bolus. Stiffness of neck and extension of head during recovery
@@@ - Paddling of fore limbs on recovery

GROUP II

This group comprised of seven animals, which underwent emergency surgery (Table-2). The observations are presented in Tables 9-14.

Observations during Anaesthesia

1. Response after premedication

Administration of xylazine brought about sedation manifested by winking of eyes and incoordination of movements in all the animals along with lowering of head and neck. Three animals vomited. Attempts to vomit were noticed in two animals. Dribbling of urine was noticed in one animal.

The animals assumed sternal recumbency by 1.90 ± 0.22 min. and lateral recumbency by 3.40 ± 0.15 min. after administration of xylazine and atropine.

2. Response after propofol administration

Breath holding for 15 - 25 seconds was observed in three animals (B1, B4 and B5) during induction of general anaesthesia with propofol. It was then followed by deep inspiration later by shallow breathing.

Palpebral reflex was seen abolished only in one animal (B3) during induction. In all other animals the palpebral reflex persisted and was sluggish throughout the period of maintenance of anaesthesia.

Eye ball rolled down during induction and remained in that position throughout the period of anaesthesia in all animals except one (B2), in which the eye ball rolled down and returned to central position on induction and then rolled down and remained there during maintenance.

The jaw muscles were relaxed and permitted endotracheal intubation in all the animals. Pedal reflex was seen abolished in all animals on induction of anaesthesia with propofol. Relaxation of abdominal muscles and limbs was good in all the animals.

Respiratory arrest occurred in one animal (B5) on administration of first incremental bolus.

Hiccough was noticed in A4 on administration of second incremental bolus.

Seizure like movements - rigidity and stiffness of forelimb and neck – (after one hour of maintenance, before recovery) was noticed in one animal (B1). Shivering was noticed during recovery also in this animal. Shivering was observed when anaesthesia lightened off after each incremental bolus in one animal (B4). This had disappeared after recovery.

3. Induction dose and time

Induction dose of propofol was 5.04 ± 0.99 mg/kg body weight and induction time was 3.21 ± 0.83 minutes.

4. Duration of anaesthesia after induction bolus

Duration of anaesthesia after initial bolus was 18.54 ± 1.64 minutes.

5. Average incremental dose and duration of effect

Average incremental dose needed was 2.98 ± 0.50 mg/kg. Average duration of effect of incremental bolus was 16.85 ± 2.71 minutes.

6. Rejection of endotracheal tube

Animals rejected the endotracheal tube by 22.89 ± 3.95 min after last incremental bolus.

Lifting of head after recovery was observed in 2.29 ± 0.46 min. Animals resumed sternal recumbency by 8.5 ± 1.18 min and was able to stand by 20.9 ± 1.25 min after recovery. The gait of the animal became apparently normal by 27.2 ± 3.06 minutes.

Physiological observations

Respiration rate (per minute) was 51.49 ± 11.72 and 18.43 ± 1.80 before and after premedication respectively and 15.71 ± 2.88 at 15 min. after induction with propofol. There was a significant decrease in respiration rate after premedication and at 15 min after induction with propofol ($p<0.05$).

Pulse rate (per minute) was 124.57 ± 7.01 and 85.14 ± 6.47 before and after premedication respectively and 92.86 ± 7.82 at 15 min. after induction. There was significant decrease in pulse rate after premedication ($p<0.05$) and at 15 min. after induction ($p<0.01$).

Rectal temperature (^0C) was 39.01 ± 0.30 and 39.03 ± 0.20 before and after administration of premedication respectively and 38.43 ± 0.35 at 15 min after induction. The changes were marginal and within normal range.

Heart rate (per/min) was 137.86 ± 6.95 and 98.29 ± 10.10 before and after premedication and 112.14 ± 9.50 at 15 min after induction. The decrease was significant ($p<0.01$) after premedication and at 15 min after induction with propofol ($p<0.05$).

Electrocardiogram

Before premedication

Wandering pacemaker – Wandering pacemaker was noticed in one dog (B7)

ST segment – ST coving was noticed in two dogs (B2 and B6)

After premedication –

Wandering Pacemaker – Wandering pacemaker was noticed in two animals (B1 and B2) after premedication.

Heart rate – Heart rate reduced in all animals after premedication. Sinus bradycardia was noticed in one dog (B4).

QRS – There was increase in the duration of QRS in one animal (B7)

ST segment – ST coving (Fig.4) was observed in two dogs (B2 and B6).

After induction

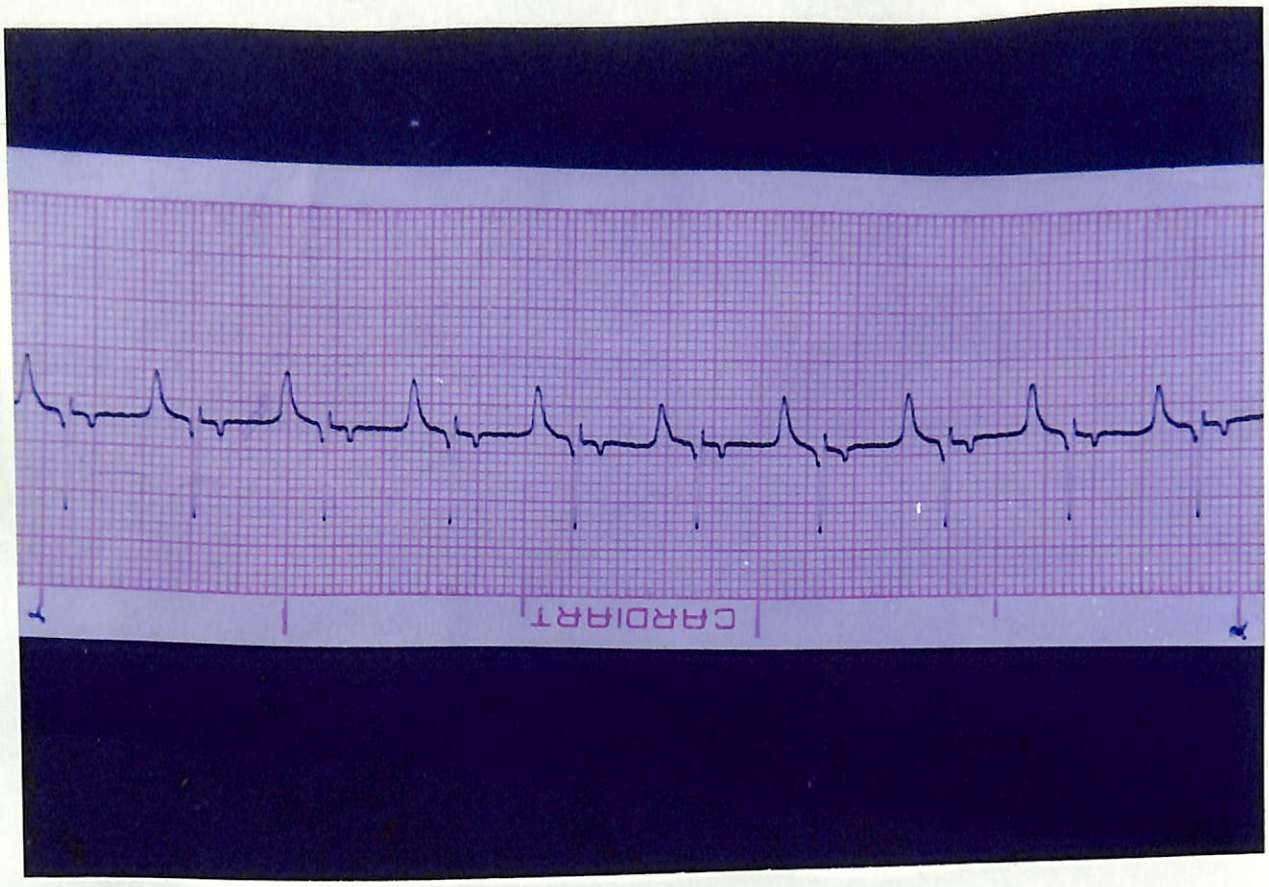
Heart rate – There was increase in heart rate from that after premedication in four animals (B1, B2, B4 and B5) and decrease in two animals (B3 and B7).

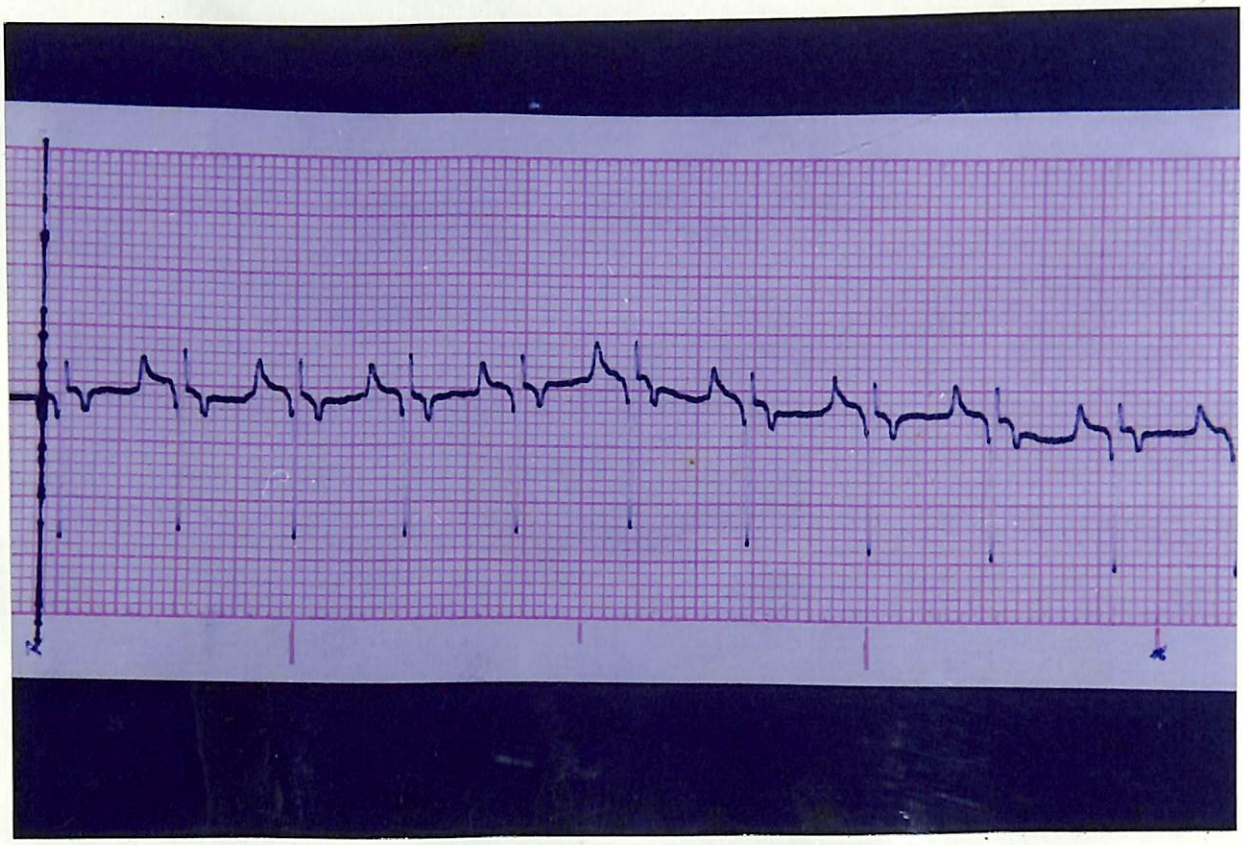
T wave – T wave was greater than ¼ R wave (Fig.5) at 30 min. post induction with propofol in one dog (B6) and the duration was 0.08 sec.

ST segment – ST coving (Fig.5) was seen throughout the period of observation in two dogs (B2 and B6).

Systolic blood pressure

Systolic blood pressure (mm Hg) was 193.43 ± 12.12 and 176.57 ± 16.31 before and after premedication respectively and 202.0 ± 16.68 at 15 min. after induction. There was a significant decrease in systolic blood pressure after premedication. The value at 15 min. after induction was higher but within normal range.


CARDIART



Diastolic blood pressure

Diastolic blood pressure (mm Hg) was 149.0 ± 7.27 and 136.0 ± 16.21 before and after premedication respectively and 166.57 ± 19.84 at 15 min. after induction. The changes were within normal range.

Mean arterial blood pressure

Mean arterial pressure (mm Hg) was 171.21 ± 9.00 and 156.29 ± 16.10 before and after premedication respectively and 184.29 ± 18.23 at 15 min. after induction with propofol. The changes observed were within normal range.

Haemogram

Erythrocyte sedimentation rate (mm/30 min) was 8.43 ± 6.45 and 13.57 ± 7.11 before and after premedication and 10.71 ± 6.41 at 20 min. after induction with propofol. There was a marginal increase within normal range.

Packed cell volume (per cent) was 35.14 ± 2.98 and 30.86 ± 4.26 before and after premedication and 30.71 ± 3.18 at 20 min. after induction with propofol. The decrease seen after premedication and at 20 min. after induction was significant ($p<0.05$).

Haemoglobin concentration (g/dl) was 11.09 ± 0.82 and 8.97 ± 0.90 before and after premedication and 9.17 ± 0.63 at 20 min. after induction with

propofol. The decrease in haemoglobin concentration noticed after premedication and at 20 min. after induction was significant ($p<0.01$) respectively.

Erythrocyte count (x $10^6/mm^3$) was 5.48 ± 0.34 and 4.71 ± 0.34 before and after premedication and 4.90 ± 0.35 at 20 min. after induction with propofol. There was significant decrease in the count after premedication ($p<0.01$) and at 20 min. after induction with propofol ($p<0.05$).

Total leukocyte count (x $10^3/mm^3$) was 18.49 ± 3.31 and 16.01 ± 2.46 before and after premedication and 18.72 ± 3.54 at 20 min. after induction with propofol. The decrease seen after premedication and the increase seen at 20 min. after induction was not significant.

Neutrophil count (per cent) was 72.06 ± 1.74 and 68.46 ± 1.45 before and after premedication and 70.61 ± 1.61 at 20 minutes after induction with propofol. There was a slight decrease in the count after premedication

and it gradually increased to near normal value at 20 min. after induction with propofol. The changes were marginal and within normal range.

Lymphocyte count (per cent) was 26.19 ± 2.07 and 29.73 ± 1.83 before and after premedication and 27.5 ± 2.14 at 20 min after induction with propofol. There was slight increase in the count after premedication then decreased to near normal at 20 min. after induction with propofol. The changes were marginal and were within physiological limits.

Monocyte count (per cent) was 1.0 ± 0.39 and 0.89 ± 0.37 before and after premedication and 1.11 ± 0.48 at 20 min after induction with propofol. The changes were marginal and within normal range.

Eosinophil count (per cent)was 0.76 ± 0.36 and 0.79 ± 0.49 before and after premedication and 0.56 ± 0.39 at 20 min after induction with propofol. The changes were marginal and within normal range.

The changes in basophil count (per cent) were not significant.

Serum constituents

Serum sodium concentration (mEq/l) was 73.60 ± 0.60 and 73.09 ± 0.78 before and after premedication and 72.83 ± 0.55 at 20 min after induction with propofol. The changes observed were marginal.

Serum potassium concentration (mEq/l) was 2.66 ± 0.15 and 2.63 ± 0.12 before and after premedication and 2.71 ± 0.11 at 20 min after induction with propofol. The changes were marginal.

Total serum protein (g/dl) was 7.1 ± 0.60 and 7.19 ± 0.66 before and after premedication and 7.23 ± 0.33 on the seventh postoperative day. The variations observed were marginal and within normal range.

Albumin/Globulin (A/G) ratio was 0.76 ± 0.07 and 0.73 ± 0.11 before and after premedication and 0.66 ± 0.08 on the seventh post operative day. The changes were marginal.

Table-9. Induction time, duration of anaesthesia and time of recovery after xylazine-atropine premedication and propofol anaesthesia in Group II animals (n=7)

Assumption of sternal recumbency after preanaesthetic medication (min)	1.90 ± 0.22
Assumption of lateral recumbency after preanaesthetic medication (min)	3.40 ± 0.15
Induction dose (mg/kg) of propofol administered	5.04 ± 0.99
Induction time (min.)	3.21 ± 0.83
Duration of anaesthesia after initial bolus (min.)	18.54 ± 1.64
Average incremental dose of propofol (mg/kg) administered	2.98 ± 0.50
Average duration of anaesthetic effect of incremental dose (min.)	16.85 ± 2.71
Rejection of endotracheal tube after last bolus (min.)	22.89 ± 3.95
Head lifting after recovery (min.)	2.29 ± 0.46
Assumption of sternal recumbency after recovery (min.)	8.5 ± 1.18
Standing after recovery (min.)	20.9 ± 1.25
Walking after recovery (min.)	27.2 ± 3.06

Table-10. Effect of administration of propofol with xylazine-atropine premedication on respiration rate, pulse rate, temperature and heart rate in Group II animals (Mean ± SE) (n=7)

Parameter	Before premedication	After premedication with xylazine and atropine	15 minutes after induction with propofol
Respiration (per/min)	51.49 ± 11.72	18.43 ± 1.80*	15.71 ± 2.88*
Pulse (per/min)	124.57 ± 7.01	85.14 ± 6.47*	92.86 ± 7.82**
Temperature (^{0}C)	39.01 ± 0.30	39.03 ± 0.20	38.43 ± 0.35
Heart rate (per/min)	137.86 ± 6.95	98.29 ± 10.10**	112.14 ± 9.50*

* - Significant at 5% level as compared to value before premedication
** - Significant at 1% level as compared to value before premedication

Table-11. Effect of administration of propofol with xylazine-atropine premedication on systolic, diastolic and mean arterial blood pressures in Group II animals (Mean ± SE) (n=7)

Parameter	Before premedication	After premedication with xylazine and atropine	15 minutes after induction with propofol
Systolic blood pressure (mm Hg)	193.43 ± 12.12	176.57 ± 16.31*	202.0 ± 16.68
Diastolic blood pressure (mm Hg)	149.0 ± 7.27	136.0 ± 16.21	166.57 ± 19.84
Mean blood pressure (mm Hg)	171.21 ± 9.00	156.29 ± 16.10	184.29 ± 18.23

* - Significant at 5% level as compared to value before premedication

Table-12. Effect of administration of propofol with xylazine-atropine premedication on haematological parameters in Group II animals (Mean ± SE) (n=7)

Parameter	Before premedication	After premedication with xylazine and atropine	20 minutes after induction with propofol
ESR (mm/30 min)	8.43 ± 6.45	13.57 ± 7.11	10.71 ± 6.41
PCV (per cent)	35.14 ± 2.98	30.86 ± 4.26*	30.71 ± 3.18*
Haemoglobin (g/dl)	11.09 ± 0.82	8.97 ± 0.90**	9.17 ± 0.63**
RBC (x 10^6/mm^3)	5.48 ± 0.34	4.71 ± 0.34**	4.90 ± 0.35*
TLC (x10^3/mm^3)	18.49 ± 3.31	16.01 ± 2.46	18.72 ± 3.54
Neutrophil (per cent)	72.06 ± 1.74	68.46 ± 1.45	70.61 ± 1.61
Lymphocyte (per cent)	26.19 ± 2.07	29.73 ± 1.83	27.5 ± 2.14[a]
Monocyte (per cent)	1.0 ± 0.39	0.89 ± 0.37	1.11 ± 0.48
Eosinophil (per cent)	0.76 ± 0.36	0.79 ± 0.49	0.56 ± 0.39
Basophil (per cent)	0.14 ± 0.13	0.10 ± 0.10	0

* - Significant at 5% level as compared to value before premedication
** - Significant at 1% level as compared to value before premedication
a - Significant at 5% level as compared to value after premedication

Table-13. Effect of administration of propofol with xylazine-atropine premedication on the serum biochemical parameters in Group II animals (Mean ± SE) (n=7).

Parameter	Before premedication	After premedication with xylazine and atropine	20 minutes after induction with propofol	Seventh day
Sodium (mEq/l)	73.60 ± 0.60	73.09 ± 0.78	72.83 ± 0.55	--
Potassium (mEq/l)	2.66 ± 0.15	2.63 ± 0.12	2.71 ± 0.11	--
Total protein (g/dl)	7.1 ± 0.60	7.19 ± 0.66	--	7.23 ± 0.33
A/G Ratio	0.76 ± 0.07	0.73 ± 0.11	--	0.66 ± 0.08

Table-14. Signs observed during induction, maintenance and recovery in Group II animals (n=7)

	Breath holding during induction	Palpebral reflex	Status of eyeball	Pedal reflex	Relaxation of jaw muscles	Relaxation of abdominal muscles	Seizure like movements
A1	-	+	X	Abolished	Good	Good	**
A2	For 20 seconds	+	XX	Abolished	Good	Good	--
A3	--	Abolished	X	Abolished	Good	Good	--
A4	For 15 seconds, HC	+	X	Abolished	Good	Good	***
A5	For 25 seconds, RA	+	X	Abolished	Good	Good	--
A6	--	+	X	Abolished	Good	Good	--
A7	--	+	X	Abolished	Good	Good	--
A8	--	+	X	Abolished	Good	Good	--

HC - Hiccough after second incremental bolus
RA - Respiratory arrest on administration of first increment
\+ - Sluggish throughout anaesthetic period
X - Rolled down during induction and remained in that position throughout the anaesthetic period
XX - Rolled down and returned to centre on induction, then rolled down and remained there throughout the anaesthetic period
** - Rigidity and stiffness of forelimb and neck towards end of anaesthetic period; Shivering during recovery
*** - Shivering towards end of anaesthetic period provided by each incremental bolus

Discussion

DISCUSSION

The study was conducted in 15 dogs of different breeds of either sex, presented to the clinics of the college for various surgical interventions. These animals were divided into two groups viz. group I which consisted of eight apparently healthy dogs presented for elective surgery and group II which consisted of seven dogs presented for emergency surgery.

All the animals were premedicated with atropine sulphate @ 0.04 mg/kg body weight IM and xylazine @ 1 mg/kg IM. Ten minutes after premedication, general anaesthesia was effected with intravenous injection of propofol and was maintained with propofol as and when required.

Evaluation of anaesthesia for surgery included continuous monitoring of clinical signs, physiological and haematological parameters. In veterinary surgery, the transformation of the conscious animal to the quiet state of anaesthesia, duration of anaesthesia and the uneventful, early recovery are very important for the clinician. Experimental studies of propofol in premedicated dogs revealed it to be a safe anaesthetic without much side effects. But the effects of propofol along with xylazine premedication were not much evaluated in clinical surgery. Hence, the observations during anaesthesia and recovery were studied to evaluate the anaesthetic effect of propofol.

Observations during Anaesthesia

Response after premedication

Administration of xylazine-atropine premedication brought about sedation manifested by winking of eyes and incoordination of movements along with lowering of head and neck in all the animals of both the groups.

The time taken by animals of group II to assume sternal and lateral recumbency was significantly lesser ($p<0.01$) than that in group I.

Response after propofol administration

Breath holding for 15 seconds was noticed in animals of group I during induction, while it was 15-25 seconds in group II. Hall and Chambers (1987) observed apnoea extending upto 20 seconds when anaesthesia was induced with propofol. Watkins *et al.* (1987) observed apnoea upto 30 seconds when a calculated bolus dose was administered intravenously and if the same dose was administered slowly the apnoea extended from 10 to 40 seconds. David (1992) observed apnoea period ranging from 28 to 40 seconds when anaesthesia was induced with propofol in triflupromazine premedicated dogs.

Palpebral reflex was not abolished during induction in both the groups and it was sluggish throughout maintenance of anaesthesia. Aitkenhead and Smith (1990) stated that there is a delay in disappearance of the eyelash reflex in humans, used normally as a sign of unconsciousness after administration of barbiturates. Eyeball did not maintain the central position on induction of

anaesthesia and during the maintenance period in both the groups. This was similar to that observed by Hall and Chambers (1987) where surgical anaesthesia with continuous intravenous infusion of propofol was associated with downward rotation of the eyeball so that the pupil was not visible for inspection, and eyelash reflex was sluggish.

Pedal reflex was abolished in all the animals of both the groups on induction. Kim *et al.* (1999) reported the loss of toe-web needle prick response in xylazine premedicated dogs anaesthetised with propofol.

Jaw muscle tone disappeared on induction. Relaxation of abdominal muscles and limbs were good in both the groups. Hall and Chambers (1987) also reported that relaxation of jaw muscle was good with propofol anaesthesia. Anal sphincter relaxation was noticed in two dogs of group I.

Urination during induction of anaesthesia and dribbling of urine throughout the period of maintenance were observed in two animals of group I. Defecation was noticed in one dog during maintenance. These were not observed in group II. Respiratory arrest occurred in one dog of group II during administration of incremental bolus. Hiccough was noticed in one dog of group II after administration of incremental bolus. Persistent coughing, jerky respiratory movements and hiccough during continuous intravenous anaesthesia using propofol was reported by Hall and Chambers (1987).

Seizure like movements observed during maintenance and while in recovery did not persist long. It disappeared after recovery. Similar findings were also reported by Hall and Chambers (1987).

Induction dose

In the present study the induction dose of propofol needed to effect anaesthesia was 5.09 ± 0.59 mg/kg and 5.04 ± 0.99 mg/kg in group I and in group II respectively. There was not much difference in the induction dose between the groups. Morgan and Legge (1989) induced anaesthesia with 4.50 ± 1.53 mg/kg body weight, Weaver and Raptopoulas (1990) with 3.60 ± 1.40 mg/kg and David (1992) induced anaesthesia with 5.02 mg/kg in premedicated dogs. Robinson *et al.* (1995) stated that the induction dose rate of propofol after xylazine premedication was 3 mg/kg. Morgan and Legge (1989) reported that when a new anaesthetic is used for the first time, a period of adaptation and familiarisation is required for developing preferred administration technique like administration to effect, selection of an appropriate dose rate based on previous experience and injection as single bolus as quickly as possible which may further bring down the dose.

Induction time

The time taken for induction of anaesthesia with propofol was 4.20 ± 1.08 min in group I animals and 3.21 ± 0.83 min in group II animals. This is longer than the time reported previously. This concurs with the fact that during

the initial trial of a new anaesthetic, it will be administered slowly taking more time for induction. The animals of group II took less time to be anaesthetised when compared to group I. It may be because of the already compromised state. Hull (1986) reported that the induction of anaesthesia with propofol would take one circulation time. Propofol is a lipid soluble drug, hence the plasma free fraction concentration would be high and the induction is attained within one to two minutes. In premedicated dogs, the mean induction time is lesser because of the adjunct effect. David (1992) observed one minute for induction of anaesthesia with propofol in premedicated dogs.

Duration of anaesthesia after induction bolus

The duration of anaesthesia after initial bolus was 14.03 ± 2.04 min in group I animals and 18.54 ± 1.64 in group II animals. There was no significant difference between the two. The longer duration of anaesthesia can be attributed to the adjunct effect provided by xylazine. Kim *et al.* (1999) also noticed longer duration of anaesthesia with propofol when xylazine was premedicated @ 1 mg/kg im than when it was given at the rate of 0.55 mg/kg. Duration of anaesthesia in animals of group II was more than that of group I and can be attributed to the lower clearance or metabolism in an already compromised system. Genevois *et al.* (1988) observed the duration of surgical anaesthesia in dogs for a period of 4 minutes 42 seconds in unpremedicated dogs. David (1992) reported the duration of anaesthesia of 4 minutes 28 seconds for unpremedicated dogs, and 9 minutes 30 seconds for premedicated dogs. The shorter duration of

surgical anaesthesia may be attributed to high plasma clearance (Hull, 1986) and metabolism into sulphate and glucuronic conjugates of propofol. These metabolic products have no hypnotic properties (Dundee, 1989). When triflupromazine was used as a premedicant (David, 1992), the duration of anaesthesia was increased and may be attributed to the prolonged and intensified action of triflupromazine as an adjunct to anaesthesia (Jones *et al.*, 1981).

Average incremental dose

The average incremental dose of propofol administered was 2.78 ± 0.45 mg/kg in group I and 2.98 ± 0.50 in group II animals. This was almost half of the induction bolus. This finding was similar to that reported by Morgan and Legge (1989). The average incremental dose needed by group II was slightly higher than group I, since the group II animals required deeper planes for prolonged surgical procedures.

Average duration of effect of incremental bolus

The average duration of effect of incremental dose obtained in the present study was 10.04 ± 0.75 min in group I and 16.85 ± 2.71 min in group II animals. This was much higher than that reported earlier by Morgan and Legge (1989) and can be due to the increased dose administered and the adjunct effect provided by xylazine. The increased duration of effect in group II animals ($p<0.05$) compared to group I animals may also be attributed to decreased clearance in sick animals.

Rejection of endotracheal tube (recovery)

Dogs in group I showed arousal by rejection of endotracheal tube 12.56 ± 1.57 min after last bolus while in group II it was 22.89 ± 3.95 min after last bolus. The arousal time was higher ($p<0.05$) compared to group I. The arousal time observed by Thurmon *et al.* (1995) where dogs were premedicated with medetomidine (@ 15µg/kg) and propofol given iv (@ 2 mg/kg) was 24.7 ± 3.7 min. Genevois *et al.* (1988) observed that propofol given as single iv injection at an average dosage of 8 mg/kg in unpremedicated dogs gave an average of 4 min 42 sec of analgesia and 7 min 18 sec before the patient began to raise its head. The early recovery in the unpremedicated group can be attributed to the less impairment of the motor component and of the higher discriminatory cerebral functions (Logan *et al.*, 1985) and to the high plasma clearance (Hull, 1986). In the premedicated animals the prolonged duration of recovery may be attributed to the residual depressive effect of the tranquilizer.

Recovery parameters

Lifting of head after recovery took 2.41 ± 0.58 min in group I and 2.29 ± 0.46 min in group II animals. The time taken by animals of group II was slightly lesser than that of group I.

Animals of group I resumed sternal recumbency by 7.94 ± 1.42 min and of group II by 8.5 ± 1.18 min. Prolonged time (34.6 ± 9.2 min) for resuming of sternal recumbency was recorded by Thurmon *et al.* (1995).

Animals of group I were able to stand by 14.72 ± 1.63 min after recovery while it was 20.9 ± 1.25 min for group II. Standing time observed by Thurmon *et al.* (1995) was 38.1 ± 9.2 min. after arousal.

The gait of the animals of group I became apparently normal by 19.69 ± 1.55 minutes, while it took 27.2 ± 3.06 minutes for group II animals.

Physiological observation

Respiration rate

There was significant decrease in respiration rate in both the groups after premedication and at 15 minutes after induction with propofol in both groups. Peshin *et al.* (1980) reported decrease in respiratory rate in dogs following IM administration of xylazine. Kim *et al.* (1999) reported significant reduction in respiratory rate following propofol administration. Genevois *et al.* (1988) observed slight respiratory depression following propofol administration in unpremedicated dogs. But in 104 premedicated dogs with atropine and acepromazine, Watkins *et al.* (1987) observed varying degree of changes in respiratory rate viz. reduction, increase and no change. David (1992) states that the higher respiratory depression during surgical anaesthesia in tranquilized dogs is due to the combined depressive effect of propofol and the premedicant.

Pulse rate

In group I, there was only a mild decrease in pulse rate after premedication, thereafter at 15 min post induction it had increased. In group II

there was significant decrease in pulse rate after premedication ($p<0.05$) and thereafter at 15 min post induction there was a mild increase but still it was significantly lower than baseline value. Watkins et al (1987) reported that a mild increase in pulse rate could be observed in dogs with slow pulse rate during propofol anaesthesia and decrease in pulse rate in animals with faster pulse rate.

Rectal temperature

There was a slight increase in temperature after premedication in both the groups. The temperature then showed a decrease 15 min after induction with propofol in both the groups. David (1992) noticed decrease in rectal temperature after premedication and during surgical anaesthesia with propofol. During anaesthesia the animals' ability to control body temperature is reduced and the animal tend to become ectothermic during anaesthesia (Bushman and Thompson, 1989). The anaesthetics also reduced the basal metabolic rate and peripheral circulation.

Heart rate

The heart rate was seen reduced after premedication and then increased at 15 min after induction with propofol in both the groups. These changes were not significant in group I. But the reduction seen after premedication in group II was highly significant and may be due to the effect of xylazine. The increase seen at 15 min after induction was not significant compared to the value after premedication but was significantly lower than the value before premedication.

Peshin *et al.* (1980) also reported significant reduction in heart rate following IM administration of xylazine in dogs. Kim *et al.* (1999) reported significant reduction in heart rate after administration of propofol in xylazine premedicated dogs.

Electrocardiogram

After premedication

Tachycardia was noticed in three animals of group I after premedication, probably due to the effect of atropine.

There was decrease in heart rate after premedication in all animals of group II. Marked decrease in heart rate with 2nd degree heart block was observed in two dogs of group I after premedication. Sinus bradycardia was observed in one dog of group II.

Wandering pacemaker was observed in two dogs after premedication in group I and II.

Ventricular pre-excitation, atrial premature contraction and increase in the duration of QRS were observed in one dog each after premedication in group I.

ST coving was observed in one dog of group I and two dogs of group II after premedication. This can be probably due to the hypoxia caused by the decrease in respiration.

After induction

At 15 min post induction, heart rate was greater than the value after premedication in all animals except one dog in group II. Tachycardia was noticed in three dogs. In group II, heart rate was greater than the value after premedication in four dogs and lesser in two dogs.

Biphasic and negative T wave was observed at 45 min. In one dog in Group I, the T wave was greater than ¼ R wave at 60 min and 75 min after induction with propofol. In group II, one dog had T wave greater than ¼ R wave at 30 min post induction. Duration was 0.08 sec.

ST coving was seen throughout the period of observation in two dogs of group II.

The increase in heart rate during anaesthesia can be attributed to the increased level of carbon dioxide in the blood. The elevation of carbon dioxide in various stages of anaesthesia could be attributed to the reduction in tidal volume, decrease in the ratio of inspiratory time to the total respiratory cycle and decrease in the functional residual capacity (Goodman *et al.*, 1987 and Sebel and Lowdon, 1989). Increased carbon dioxide tension stimulates the peripheral chemoreceptor and vasomotor centres of the medulla which in turn stimulates the sympathetic activity (Moster *et al.*, 1969). David (1992) in his study observed elevation of heart rate from the preinduction value followed by decline to normalcy during recovery. The increase in heart rate during recovery in premedicated dogs was

attributed to the prolonged effect of atropine. Anoxia during anaesthesia may also increase the heart rate.

David (1992) reported that the duration of QT interval to be less in premedicated group when compared with unpremedicated group of dogs which could be attributed to a reduction on vagal inhibition by atropine.

Systolic, diastolic and mean arterial pressure

There was reduction in systolic, diastolic and mean arterial blood pressures in both the groups after premedication. This was followed by an increase in value 15 min. after induction with propofol in both the groups. Klide *et al.* (1975) and Hsu *et al.* (1985) reported an initial increase in blood pressure followed by a decrease with intravenous administration of xylazine with and without atropine. Brussel *et al.* (1989) observed significant decrease in systolic and diastolic pressures with propofol. A fall in blood pressure during the first four min. after propofol anaesthesia was observed by Grounds *et al.* (1985), Andreev *et al.* (1988) and Dundee and Wyant (1988). But according to David (1992), there was no change in diastolic pressure and systolic pressure when propofol alone was administered as anaesthetic. But in triflupromazine premedicated group, systolic and diastolic blood pressure reduced and became stable during anaesthesia. Sebel and Lowdon (1989) stated that although the induction dose of propofol decreased the arterial pressure, the sympathetic stimulation of intubation reversed this decline, to return to the pre-induction haemodynamic status.

Haemogram

Erythrocyte sedimentation rate

Erythrocyte sedimentation rate showed a decrease after premedication in group I and an increase in group II. In both the groups there was decrease at 20 min after induction with propofol. Sear *et al.* (1985) observed fall in haemotocrit value without significant change in erythrocyte sedimentation rate. David (1992) also found similar result with propofol anaesthesia.

Packed cell volume

In group I, packed cell volume showed a significant decrease after premedication and an increase at 20 min after induction with propofol. The increase was highly significant though the value was lower than the value before premedication. In group II the PCV showed significant decrease both after premedication and at 20 min after induction with propofol. Peshin *et al.* (1980) reported slight reduction in PCV with xylazine administration in dogs. David (1992) observed decrease in PCV during anaesthesia with propofol. The reduction may be attributed to the corticosteroid response evinced by propofol (Glen *et al.* 1985).

Haemoglobin concentration

In the present study there was decrease in the haemoglobin concentration after premedication followed by an increase at 20 min after induction with propofol in both the groups. David (1992) did not find any significant change in

haemoglobin concentration in various stages of propofol anaesthesia. Similar finding was reported by Peshin *et al.* (1980) with xylazine and Sears *et al.* (1985) with propofol.

Erythrocyte count

In the present study the total erythrocyte count showed a highly significant decrease following premedication. It was followed by an increase at 20 min after induction with propofol. Peshin *et al.* (1980) reported reduction in the total erythrocyte count following xylazine administration in dogs. Sears *et al.* (1985) reported that propofol could induce anaesthesia with a fall in haematocrit value without significant fall in total erythrocyte count. According to David (1992) the mean total erythrocyte count reduced during anaesthesia.

Total leukocyte count

There was decrease in the total leukocyte count in both the groups after premedication. It was then followed by an increase to the value before premedication in both groups. Peshin *et al.* (1980) observed slight reduction in total leukocyte count following xylazine administration. Sears *et al.* (1985) and David (1992) reported that there was no significant change in total leukocyte count following propofol anaesthesia. Kim *et al.* (1999) observed that there is no significant change in the TLC in xylazine premedicated dogs anaesthetised with propofol.

Differential leukocyte Count

Neutrophil count was significantly high ($p<0.01$) both after premedication and at 20 min after induction with propofol in group I. In group II there was a slight decrease following premedication followed by an increase 20 min after propofol.

There was significant reduction in the lymphocyte count after premedication in group I followed by slight increase after induction with propofol, but it was still lesser than the value before premedication. In group II there was increase in count after premedication followed by decrease after induction.

Eosinophil count showed significant reduction after premedication. Changes in monocyte and basophil counts were not significant.

Peshin *et al.* (1980) reported decrease in lymphocyte count with corresponding increase in neutrophil count following xylazine administration. David (1992) stated that there was neutrophilia with corresponding lymphopenia during propofol anaesthesia. Kim *et al.* (1999) observed no significant change in TLC with xylazine-propofol anaesthesia in dogs.

Serum constituents

There was increase in the serum sodium concentration both after premedication and after induction with propofol in group I. But in group II there was slight decrease in sodium and potassium concentration after premedication

followed by an increase 20 min after induction with propofol. Peshin *et al.* (1980) observed mild increase in serum sodium and decrease in serum potassium after xylazine administration in dogs.

An increase in total protein was observed after premedication in both the groups. The Albumin/Globulin ratio was seen decreased after premedication but it was not significant. On the seventh day, all values had returned to baseline. Kim *et al.* (1999) also observed significant increase in total protein and albumin after anaesthesia with xylazine and propofol in dogs. But David (1992) observed no change in total serum protein in different stages of propofol anaesthesia in dogs.

Summary

SUMMARY

The study was conducted in 15 dogs of different breeds of either sex, presented to the clinics of the college for various surgical interventions. These animals were divided into two groups viz. group I, which consisted of eight apparently healthy dogs, presented for planned surgery and group II, which consisted of seven dogs presented for emergency surgery.

All the animals were premedicated with atropine sulphate @ 0.04 mg/kg body weight IM immediately followed by xylazine @ 1 mg/kg body weight IM. Ten minutes later, general anaesthesia was induced with intravenous administration of one percent solution of propofol "to effect" and maintained by incremental dose(s) of propofol as bolus injection(s).

Administration of xylazine-atropine premedication brought about sedation manifested by winking of eyes and incoordination of movements along with lowering of head and neck in all the animals of both the groups.

The time taken by animals of group II to assume sternal and lateral recumbency was significantly lesser ($p<0.01$) than that in group I.

Breath holding for 15 sec was noticed in animals of group I during induction, while it was 15-25 sec in group II.

Palpebral reflex did not abolish during induction in both the groups and it was sluggish throughout the maintenance period. Eyeball did not maintain the

central position on induction of anaesthesia and during the maintenance period in both the groups.

Pedal reflex abolished in all the animals of both groups on induction. Jaw muscle tone disappeared on induction. Relaxation of abdominal muscles and limbs were good in both the groups. Anal sphincter relaxation was noticed in two dogs of group I.

Two animals of group I urinated during induction of anaesthesia and dribbled urine throughout the maintenance period. Defecation was noticed in one dog during maintenance period. These were not noticed in group II.

Respiratory arrest occurred in one dog of group II during administration of incremental bolus. Hiccough was noticed in one dog of group II after administration of incremental bolus.

The induction dose of propofol needed "to effect" anaesthesia was 5.09 ± 0.59 mg/kg and 5.04 ± 0.99 mg/kg in group I and in group II respectively. There was not much difference in the induction dose between the groups.

The time taken for induction of anaesthesia with propofol was 4.20 ± 1.08 min in group I animals and 3.21 ± 0.83 min in group II animals.

The duration of anaesthesia after initial bolus was 14.03 ± 2.04 min in group I animals and 18.54 ± 1.64 in group II animals.

The average incremental dose of propofol administered was 2.78 ± 0.45 mg/kg in group I and 2.98 ± 0.50 in group II animals.

The average duration of effect of incremental dose obtained in the present study was 10.04 ± 0.75 min in group I and 16.85 ± 2.71 min in group II animals.

Dogs in group I showed arousal by rejection of endotracheal tube 12.56 ± 1.57 min after last bolus while in group II it was 22.89 ± 3.95 min after last bolus.

Lifting of head after rejection of endotracheal tube took 2.41 ± 0.58 min in group I and 2.29 ± 0.46 min in group II animals.

Animals of group I resumed sternal recumbency by 7.94 ± 1.42 min and of group II by 8.5 ± 1.18 min.

Animals of group I were able to stand by 14.72 ± 1.63 min after recovery while it took 20.9 ± 1.25 min for group II.

The gait of the animals of group I became apparently normal by 19.69 ± 1.55 minutes, while it took 27.2 ± 3.06 minutes for group II animals.

There was significant decrease in respiration rate in both the groups after premedication and at 15 minutes after induction with propofol in both groups.

In group I, there was only a mild decrease in pulse rate after premedication, thereafter at 15 min post induction it had increased. In group II

there was significant decrease in pulse rate after premedication ($p<0.05$) and thereafter at 15 min post induction there was a mild increase but still it was significantly lower than baseline value.

There was a slight increase in body temperature after premedication in both the groups. Fall in body temperature was observed 15 min after induction with propofol in both the groups.

The heart rate reduced after premedication and then increased at 15 min after induction with propofol in both groups.

Tachycardia was noticed in three animals of group I after premedication. There was decrease in heart rate after premedication in all animals of group II. Marked decrease in heart rate with 2nd degree heart block was observed in two dogs of group I after premedication. Sinus bradycardia was observed in one dog of group II.

Wandering pacemaker was observed in two dogs after premedication in group I and II.

Ventricular pre-excitation was noticed after premedication in one dog of group I. Atrial premature contraction was noticed in one dog of group I, after premedication. Increase in the duration of QRS observed after premedication in one dog of group I.

ST coving observed in one dog of group I and two dogs of group II after premedication. The dogs of group II already had ST coving before premedication.

At 15 min post induction, heart rate was greater than the after premedication value in all animals except one dog in group II. Tachycardia was noticed in three dogs of group I after induction. In group II, heart rate was greater than the value after premedication in four dogs and lesser in two dogs after induction.

T wave was biphasic at 45 min. and negative and more than ¼ R wave at 60 min. and 75 min. after induction in one dog of group I. T wave was greater than ¼ R wave and of 0.08 seconds duration at 30 min. post induction with propofol in one dog of group II.

ST coving was seen throughout the period of observation in two dogs of group II.

There was reduction in systolic, diastolic and mean arterial blood pressures in both the groups after premedication. But 15 minutes after induction with propofol there was an increase above the before premedication value in both the groups.

Marginal decrease in the erythrocyte sedimentation rate was noticed in the animals of group I both after premedication and induction, while in group II there

was marginal increase after premedication followed by slight decrease after induction.

In group I, packed cell volume showed a significant decrease after premedication and an increase at 20 min after induction with propofol. The increase was highly significant but was still lower than the before premedication value. In group II the PCV showed significant decrease both after premedication and at 20 min after induction with propofol.

There was decrease in the Haemoglobin concentration after premedication followed by an increase at 20 min after induction with propofol in both the groups.

The total erythrocyte count showed a highly significant decrease following premedication. It was followed by an increase at 20 min after induction with propofol.

There was decrease in the total leukocyte count in both the groups after premedication. It was then followed by an increase to before premedication value in both groups.

Neutrophil count was significantly high ($p<0.01$) both after premedication and at 20 min after induction with propofol in group I. In group II there was a slight decrease following premedication followed by an increase 20 min after propofol.

There was significant reduction in the lymphocyte count after premedication in group I followed by a slight increase after induction with propofol, but it was still below the value before premedication. In group II there was increase after premedication followed by decrease after induction, but it was above the value before premedication.

Eosinophil count showed significant reduction after premedication. Changes in monocyte and basophil counts were not significant.

There was increase in the serum sodium concentration both after premedication and after induction with propofol in group I. But in group II there was a slight decrease in sodium and potassium concentration after premedication followed by an increase 20 min after induction with propofol.

An increase in serum total protein was observed after premedication in both groups. The Albumin/Globulin ratio was decreased after premedication, though not significant. On the seventh day all values had returned to normal.

Based on the observations, the following conclusions could be drawn:

1. Atropine and xylazine were found to be a good preanaesthetic for propofol anaesthesia in dogs.

2. Propofol under atropine-xylazine premedication provided smooth induction of anaesthesia and was safe for maintenance of sufficient duration with incremental doses for surgery in both healthy and compromised animals.

3. Abolishment of palpebral reflex and position of eye ball could not be taken as a criteria for assessing the depth of anaesthesia with this combination.

4. There was not much difference in the induction dose between the two groups of dogs. Average incremental dose of propofol needed worked out to around half of the induction dose.

5. Recovery from xylazine-propofol anaesthesia was rapid, smooth and uneventful regardless of the number of incremental boli given for maintenance of anaesthesia.

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CLINICAL EVALUATION OF XYLAZINE-PROPOFOL ANAESTHESIA IN DOGS

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ABSTRACT OF THE THESIS

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ABSTRACT

The study was undertaken to evaluate the anaesthetic effect of propofol in xylazine premedicated canine surgical patients.

Fifteen dogs of different breeds of either sex were divided into two groups. Group I consisted of eight apparently healthy dogs presented for elective surgery, and group II consisted of seven dogs presented for emergency surgery.

All the animals were premedicated with atropine sulphate @ 0.04 mg/kg body weight IM and xylazine @ 1 mg/kg IM. Ten minutes later, general anaesthesia was effected with intravenous injection of 1% w/v propofol and was maintained with incremental dose(s) of propofol as intermittent boli as and when required.

Palpebral reflex was sluggish in both groups during induction and throughout the period of maintenance. Eyeball rolled down during induction and remained in that position throughout the period of maintenance.

The duration of anaesthesia after initial bolus was 14.03 ± 2.04 min. in group I and 18.54 ± 1.64 min. in group II. The average incremental dose of propofol needed was 2.78 ± 0.45 mg/kg in group I and 2.98 ± 0.50 mg/kg in group II. The average duration of effect of incremental dose obtained was 10.04 ± 0.75 min. in group I and 16.85 ± 2.71 min. in group II.

Animals of group I were able to stand by 14.72 ± 1.63 min. after recovery while it was 20.9 ± 1.25 min. in group II. The gait of the animals of group I became apparently normal by 19.69 ± 1.55 minutes, while it was 27.2 ± 3.06 minutes in group II animals.

Respiration rate showed significant decrease in both the groups after premedication and at 15 minutes after induction with propofol. Pulse rate and heart rate decreased after premedication and increased on induction with propofol. Electrocardiographic changes were transient. There was decrease in haemoglobin concentration after premedication, which increased on induction in both groups. Total erythrocyte count decreased on premedication and increased on induction. Total leukocyte count decreased after premedication followed by an increase after induction. Neutrophilia was observed both after premedication and on induction with propofol in group I, where as in group II neutrophil count showed a decrease on premedication which increased after induction. Lymphocyte count decreased after premedication and increased after induction in group I. But in group II lymphocyte count showed an increase after premedication, which decreased on induction of anaesthesia.

Serum sodium and potassium concentrations, total serum protein content and albumin/globulin ratio did not show any significant change during the study..

Propofol under atropine-xylazine premedication was found to be an effective and safe anaesthetic for induction and maintenance of anaesthesia for surgery in both healthy and compromised dogs with less side effects.