GENERAL ANAESTHESIA IN DOGS WITH TILETAMINE - ZOLAZEPAM

By

K. RAJANKUTTY

THESIS

Submitted in partial fulfilment of the requirement for the degree

Doctor of Philosophy

Faculty of Veterinary and Animal Sciences

KERALA AGRICULTURAL UNIVERSITY

Department of Surgery

COLLEGE OF VETERINARY AND ANIMAL SCIENCES

MANNUTHY, THRISSUR

1995

DECLARATION

I hereby declare that the thesis entitled "GENERAL ANAESTHESIA IN DOGS WITH TILETAMINE ZOLAZEPAM" is a bonafide record of research work done by me during the course of research work 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

Mannuthy

K RAJANKUTTY

7 12 1995

CERTIFICATE

Certified that this thesis entitled "GENERAL ANAESTHESIA IN DOGS WITH TILETAMINE-ZOLAZEPAM" is a record of research work done independently by Sri K Rajankutty under my guidance and supervision and that it has not previously formed the basis for the award of any degree, fellowship or associateship to him

Dr K N Muraleedharan Nayar
(Chairman, Advisory Committee)
Professor and Head i/c
Department of Surgery
College of Veterinary and
Animal Sciences
Mannuthy

Mannuthy,

7 12 1995

CERTIFICATE

We the undersigned members of the Advisory Committee of **Sri K Rajankutty** a candidate for the degree of Doctor of Philosophy in Veterinary Surgery, agree that the thesis entitled **"GENERAL ANAESTHESIA IN DOGS WITH TILETAMINE-ZOLAZEPAM"** may be submitted by Sri K Rajankutty in partial fulfilment of the requirement for the degree

Dr K N Muraleedhran Nayar
Chairman Advisory Committee
Professor and Head i/c
Department of Surgery
College of Veterinary and Animal Science
Mannuthy

Dr M K Rajagopalan
Professor and Head
Department of Pharmacology
(Member)

Dr (Mrs) K V Valsala
Associate Professor
Centre of Excellence in Pathology
(Member)

Dr K R Harshan
Associate Professor
Department of Anatomy
(Member)

Dr N Gopakumar
Associate Professor
Department of Pharmacology
(Member)

External Examiner

ACKNOWLEDGEMENT

I am deeply indebted to Dr K N Muraleedharan Nayar Professor and Head i/c, Department of Surgery and Chairman of the Advisory Committee for his guidance and constant encouragement throughout the study

I wish to express my deep sense of gratitude to Dr M K Rajagopalan, Professor and Head Department of Pharmacology Dr (Mrs) K V Valsala Associate Professor Centre of Excellence in Pathology, Dr K R Harshan Associate Professor, Department of Anatomy and Dr N Gopakumar Associate Proressor Department of Pharmacology for their valuable help and advice at various stages of work as members of the Advisory Committee

I express my sincere and heartfelt thanks to Dr P O George former Professor and Head Department of Surgery and former member of the Advisory Committee for his constant encouragement and valuable suggestions

I express my sincere thanks to Dr A M Jalaluddin former Professor of Surgery and former member of the Advisory Committee for his guidance and suggestions

My sincere thanks are due to Dr S Raveendran Nayar and Dr C Abraham Varkey Professors of the Department of Surgery

and Dr Jacob V Cheeran Professor Department of Pharmacology for their kind help

I am thankful to Dr (Mrs) T Sarada Amma Associate Professor Department of Surgery, Dr T P Balagopalan and Dr C B Devanand Assistant Professors Department of Surgery Dr David J Suresh Dr C Venkatesan and Dr (Ms) Angamuthu Jayasudha Post Graduate Scholars Department of Surgery Dr S Vigil Anbiah, Dr Vyas M Shingatgri and Dr Jacob Alexander Post Graduate Scholars, Centre of Excellence in Pathology and Dr P Prabakaran, Post Graduate Scholar Department of Nutrition for their constant assistance rendered to me during the entire period of the research work

I wish to express my sincere thanks to Sri M Nandakumaran Associate Professor, Department of Nutrition for the help rendered in laboratory work and Smt K P Santhabhai Junior Programmer, Department of Statistics, for carrying out the statistical analysis of the data

I express my sincere thanks to Dr C T Thomas Professor and Head Department of Nutrition Dr K M Ramachandran Professor and Head Centre of Excellence in Pathology Dr (Mrs) Lucy Pailey Professor and Head Department of Anatomy Dr (Mrs) Sulochana Professor and Head Department of Microbiology and Dr K C George, Professor and Head Department of Statistics for the facilities provided for the work

I remember with gratitude and affection the encouragement extended to me by Dr M Krishnan Nair former Director, Veterinary Research and Education and Late Dr G Nirmalan, former Dean i/c, College of Veterinary and Animal Sciences, Mannuthy

My sincere thanks are due to Dr A Rajan Dean College of Veterinary and Animal Sciences, Mannuthy for the facilities provided and the authorities of Kerala Agricultural University for granting me study leave for the period of my study

I am thankful to M/s Peagles, Mannuthy for the prompt and neat typing of the manuscript

I am also grateful to my parents wife daughter and son for their love and wholehearted cooperation during the study

Last but not least I wish to express my sincere thanks to all my colleagues for their support and assistance rendered to me during the course of the study

K RAJANKUTTY

CONTENTS

LIST OF TABLES

LIST OF FIGURES

Introduction

INTRODUCTION

Improvements in anaesthetic practices have contributed greatly to the refinement in surgical techniques both in man and animals The concept of anaesthesia has itself undergone changes with the newer drugs and techniques evolved Drug combination making use of the best effects of individual drugs is more acceptable now, especially in veterinary practice The anaesthetics that are administered intramuscular have become more popular in veterinary practice because of the ease of administration, wider margin of safety, and the lack of need for sophisticated equipments and facilities The chief among the agents that have thus been used are xylazine and ketamine

The dissociative anaesthetic effects of ketamine and the sedative and analgesic effects of xylazine have been found useful in the practice of surgery in animals Combined effects of the two have been acclaimed satisfactory in almost all the species of animals (Purohit *et al* 1981, Waterman 1983 Moens and Fargetton 1990 and Popilskis *et al* 1991) Combination of xylazine and ketamine with other sedatives tranquilizers and anaesthetics have also been studied (McCarty *et al* 1990 and Lin *et al* 1994) Two newly added compounds to this category are tiletamine and zolazepam

Tiletamine a dissociative anaesthetic with pharmacological properties similar to those of ketamine is chemically 2-(ethylamino)-2-(2-thienyl) cyclohexamine hydrochloride Zolazepam, a benzodiazepine with pharmacological properties similar to those of diazepam and chemically 4 (O flurophenyl)-6 8-dihydro-1, 3,8 trimethylpyrozolo 3 4 3e 1 4 diazepin-7 (1H) one monohydrochloride (Short 1987)

The combination of tiletamine-zolazepam had been reported to produce satisfactory anaesthesia in wild animals (Boever *et al* 1977 and Schobert, 1987) sheep (Lagutchik *et al* 1991 and cats (Tracy *et al* 1988 and Lendl *et al* 1991) Use of xylazine along with tiletamine-zolazepam reported to produce rapid and smooth induction prolonged duration of anaesthesia with excellent muscle relaxation and analgesia and smooth recovery in horses (Hubbell *et al* 1989 and Abrahamsen *et al* 1991) sheep (Lin *et al* 1993) and pigs (Thurmon *et al* 1989)

On perusal of the available literature the references regarding the use of tiletamine-zolazepam combination in dogs were found scanty Hence the present study was undertaken in dogs with the following objectives

1 to study the efficacy of tiletamine-zolazepam alone and with xylazine premedication, and

2 to evaluate the systemic changes consequent on the administration of these drugs

Review of Literature

REVIEW OF LITERATURE

Chen and Ensor (1968) reported calming (taming) to cataleptic (incapacitating) effect at small dose levels and general anaesthesia at large dose levels of tiletamine in cats Decreased motor activity, lack of resistance to jaw opening, and loss of biting reflex were the initial signs of calming effects Catalepsy was indicated by loss of body righting reflex without head-drop Analgesia to skin pricking and foot pad pinching and unconsciousness were the cardinal signs of surgical anaesthesia, but muscle relaxation was inadequate for certain type of surgical operation

Bennett (1969) reported that though cats were under anaesthesia with administration of tiletamine to permit surgical operation, their eyes remained open pupils were slightly dilated and palpebral and corneal reflexes persisted Occasional involuntary rotation of the globe of the eye was also observed

Krahwinkel (1970) reported the use of tiletamine hydrochloride as an incapacitating agent for a lion Swallowing reflexes persisted and hence the inhalation of the vomitus was prevented The pulse and respiration rates were within the normal range

Calderwood *et al* (1971) studied the cardiorespiratory effects of tiletamine in cats The drug produced significant respiratory depression, respiratory acidosis, and reduction in oxygen tension There was no statistically significant cardiovascular changes

Bree *et al* (1972) conducted clinical evaluation of tiletamine-zolazepam in dogs and primates and reported that the induction of anaesthesia was smooth and uneventful Rhythmic side to side head movement was noticed in dogs just before the development of cataleptic state Excellent skeletal muscle relaxation was evident Pharyngeal and palpebral reflexes were maintained in all the animals throughout the period of anaesthesia

Ward *et al* (1974) reported that tiletamine-zolazepam at the rate of 5 5-9 mg/kg bodyweight was satisfactory for anaesthesia in dogs There was evidence of pain when tiletamine-zolazepam was injected IM The swallowing and palpebral reflexes were retained, but there was no response to loud noise Defecation and urination did not occur routinely during induction Salivation was present unless suppressed by atropine The effect produced upon the cardiovascular system was less compared to other dissociative anaesthetics

Schulz and Fowler (1974) employed different doses of tiletamine zolazepam combination in chinchillas (*Chinchilla villidera*) for inducing anaesthesia Higher doses produced prolonged anaesthesia shallow respiration, considerable salivation and delayed recovery Corneal and palpebral reflexes were always present in all doses to a greater or lesser extent The effects produced were safe and predictable, with a wide margin of safety

Haskins *et al* (1975) studied the effects of tiletamine in experimental and clinical situations in cats The anaesthesia produced was characterised by good muscle relaxation eyelid closure, occasional vomition, defecation, or urination during induction and recovery Generally induction was smooth and recovery was fast but occasional hyperreflexive recoveries with much sneezing were also observed

Klide *et al* (1975) reported that in dogs the subjective sedative effects observed following xylazine administration included lying down, lack of response to the environment medial rotation of the eyes and prolapse of the nictitans, giving the appearance of asleep There was marked decrease in heart rate The blood pressure response was biphasic first an increase followed by a decrease

Smith and Pettway (1975) administered tiletamine zolazepam combination in dogs and cats at the rate of 20 mg/kg bodyweight IM and reported that the combination produced a very reliable onset (3 to 5 minutes), and convenient surgical anaesthesia with a duration greater than two hours

Euds (1976) administered tiletamine zolazepam intramuscular in non human primates and reported excellent muscle relaxation at higher doses, retention of laryngeal and pharyngeal reflexes, wide margin of safety and unremarkable recovery

Boever *et al* (1977) employed tiletamine zolazepam for chemical restraint and anaesthesia in wild and exotic carnivores Anaesthesia and muscle relaxation were adequate for various surgical procedures Adverse reactions observed were salivation, emesis and delayed recovery Excess salivation was the most common side effect, but this presented little problem since the pharyngeal and laryngeal reflexes were persisted The danger due to emesis was minimal since the swallowing reflex persisted

King *et al* (1977) used tiletamine zolazepam for the immobilization of lions and leopards A highly significant positive linear relationship was observed between the duration of anaesthesia and dosage of the drugs

Kumar and Thurmon (1977) studied the pharmacological effects of diazepam with and without premedication of atropine in goats The administration of diazepam caused reduction in respiratory rate, rectal temperature, mean arterial blood pressure and heart rate However when atropine was used as premedicant these parameters were not significantly affected, except that the heart rate was increased Prior administration of atropine caused increase in heart rate because of its vagal blocking effects The hypothermic effect of diazepam was attributed to the loss of heat as a result of depression of peripheral sympathetic system There was no significant difference in serum electrolytes (Na K and Cl) aspartate transaminase total protein, urea nitrogen and glucose with slight rise in alanine transaminase

Muir *et al* (1978) reported an increase in systolic diastolic and mean arterial pressures in horses following the administration of xylazine

Peshin *et al* (1980) observed transient bradycardia and decrease in respiratory rate in dogs following I administration of xylazine at the rate of 3 0 mg kg bodyweight 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 mycocardial hypoxia There was slight decrease in total erythrocyte and leucocyte counts packed cell volume and haemoglobin concentration 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 potassium and chloride concentrations were also observed

Colby and Sanford (1981) studied the changes in blood pressure in cats under ketamine xylazine and ketamine acepromazine anaesthesia The blood pressure was depressed by both the combinations and was more prolonged by ketamine xylazine than ketamine-acepromazine The ketamine xylazine combination presented a slow decline in the blood pressure lasting dampering effect The blood pressure did not rise until long after the animal had begun to show visible signs of recovery from anaesthesia

Nowrouzian *et al* (1981) evaluated the anaesthetic properties of ketamine and ketamine-xylazine-atropine combination in sheep The combination of ketamine xylazine and atropine appeared to give the most satisfactory results with regard to muscle relaxation, suppression of salivation urination and regurgitation as well as reflexes

Purohit *et al* (1981) evaluated the effects of xylazine and ketamine on the electrocardiogram in six horses In all the six horses xylazine administration resulted in second degree AV block and subsequent administration of ketamine abolished this effect in 4 of 6 horses

Jacobson (1983) employed ketamine xylazine combination for immobilizing springbok *(Antidorcas marsupialis)* and compared the haematologic and serum biochemical values before and after immobilization The haemotologic, serum aspartate transaminase blood urea nitrogen and chloride values before immobilization were not significantly different from those after immobilization The serum glucose and alanine transaminase values were found significantly higher in animals after immobilization, whereas the potassium value was significantly lower

Peshin and Kumar (1983) studied the haemocytological and biochemical effects of xylazine in buffalo calves and reported slight decrease in total erythrocytes leukocytes packed cell volume and haemoglobin concentration The serum aspartate transaminase and alanine transaminase values were also slightly decreased No significant change in serum electrolytes (Na K and Cl) was observed Total serum protein remained essentially unaffected

were not abolished During recovery a few dogs had mydriasis delirium 15 to 20 minute (whining, paddling) and retched or vomited froth The dogs were not responsive to auditory tactile, or visual stimulation The swallowing reflex remained but dogs had difficulty in controlling tongue movements until shortly before walking Shivering was prominent during recovery

Thurmon *et al* (1988) evaluated the anaesthetic and analgesic effects of tiletamine-zolazepam and xylazine in pigs The combination found to produce measurable sedative analgesic effect and was found effective and safe for induction and maintenance of general anaesthesia

Tracy *et al* (1988) compared the effects of intravenous and intramuscular administration of tiletamine-zolazepam in dogs and cats Intravenous administration provided faster induction to recumbency and anaesthesia in both dogs and cats and shorter recovery times in dogs

Pharmacokinetic studies conducted by Donaldson *et al* (1989) in dogs after intramuscular administration of tiletamine zolazepam revealed that zolazepam had a plasma half life of less than 1 h, whereas that of tiletamine was 1 2 h The progressive increase in muscle activity and persistent dissociation for the environment shown by the dogs

recovering from tiletamine-zolazepam reflected this difference in the plasma half-lives of tiletamine and zolazepam

Hubbell *et al* (1989) evaluated the anaesthetic and cardiopulmonary effects of xylazine in combination with tiletamine zolazepam in horses Increasing the dosage of tiletamine zolazepam significantly increased the duration of recumbency When combined with xylazine the recumbency became rapid and the anaesthesia was characterised by good muscle relaxation

Lin *et al* (1989) studied the haemodynamic response of calves to tiletamine-zolazepam anaesthesia and reported that systolic mean and diastolic arterial blood pressures and systemic vascular resistance were significantly decreased below baseline at five minutes, increased above baseline at 20 minutes and remained so throughout the 60 minutes study

Thurmon *et al* (1989) studied the effect of tiletamine-zolazepam in combination with xylazine in calves and reported that the changes in heart and respiratory rates were within clinically acceptable limits, the onset of analgesia was rapid and profound and salivation was profuse

Bush *et al* (1990) captured free ranging male koalas with intramuscular injection of tiletamine-zolazepam combination and observed rapid and smooth induction of anaesthesia lasting for

30 to 45 minutes There was no depression of heart rate or respiration Mild salivation occurred in most animals but was not a problem because the swallowing reflex was not abolished

Moens and Fargetton (1990) assessed the anaesthetic effects of ketamine combined with xylazine in dogs and opined that pinprick reflex was unsuitable for evaluating the response to pain in dogs because it was often absent long after the pedal withdrawal reflex had reappeared Muscle rigidity and stereotypic lateral head movements were observed during recovery in a few dogs

The studies carried out by Abrahamsen *et al* 1991 on horses revealed that the induction with tiletamine zolazepam after xylazine premedication was generally rapid and smooth Muscle relaxation was adequate for intubation and positioning

Brammer *et al* (1991) evaluated tiletamine zolazepam combination as an anaesthetic for rabbits and reported that there was increase in the level of blood urea nitrogen and serum creatinine following the administration of the combination Histopathological examination of kidney revealed severe renal tubular necrosis suggestive of nephrotoxicity

Farina and Fonda (1991) administered tiletamine zolazepam IM for anaesthetizing cats for various minor and major surgical operation at the dose rates of 15 mg and 20 mg kg

bodyweight With the 20 mg/kg dose surgical anaesthesia appeared in a mean time of 26 min and persisted for 59 min but the analgesic effect was not satisfactory in 43 out of 77 cats

Lagutchik *et al* (1991) evaluated the anaesthetic and cardiopulmonary effects of tiletamine-zolazepam combination in sheep The induction was rapid and smooth, and the recovery was gradual, unremarkable and characterised by prolonged period of sedation Heart rate, after a slight initial increase remained constant The mean arterial pressure after a mild decrease, gradually returned to baseline by 15 minutes and remained constant thereafter

Lin *et al* (1991) studied the haemodynamic response of calves to tiletamine-zolazepam xylazine anaesthesia Tiletamine zolazepam (4 mg/kg) and xylazine (0 1 mg/kg) were administered IV immediately after recording the baseline values for blood pressure $PaCO_2$, PaO_2 and pHa The values were again recorded at 5 10 20 30, 40, 50 and 60 minutes after the injection Changes in left ventricular work index PaO and pHa were significant Arterial blood pressure and systemic vascular resistance increased above baseline at 5 minutes and then gradually decreased below baseline at 15 minutes All the calves recovered without complication It was concluded that

tiletamine zolazepam (4 mg/kg IV)-xylazine (0 1mg/kg IV) was a safe and useful anaesthetic regimen for use in calves

Pandey *et al* (1991) studied the clinical and haematological response of diazepam (3 mg/kg IV)-ketamine (10 mg/kg IV) atropine (0 65 mg/kg) anaesthesia in canine surgical patients The combination induced anaesthesia for an average duration of 37 00 ± 3 29 min Drop in pulse rate respiration and body temperature were observed There was significant increase in total leucocyte count and neutrophil percentage while lymphocyte count dropped significantly They opined that the higher values of the leucocytes obtained in the study might be related to the adrenal corticoid released to combat stress

Popilskis *et al* (1991) compared the efficacy of ketamine Xylazine to tiletamine zolazepam-xylazine for producing surgical anaesthesia in rabbits The mean surgical anaesthesia time in the ketamine-xylazine group was 35 ± 6 min compared to 7 0 ± 8 min in the tiletamine-zolazepam xylazine group Lowering of arterial blood pressure and blood urea nitrogen values was noticed in both the groups The surgical anaesthesia produced by ketamine-xylazine was not always satisfactory but tiletamine-zolazepam-xylazine produced effective surgical anaesthesia

Singh *et al* (1991) after evaluating diazepam ketamine anaesthesia in calves had reported that the combination did not alter the plasma glucose level The plasma sodium, potassium and chloride and haematological values did not vary significantly with the combination

Stander and Morkel (1991) employed tiletamine-zolazepam for field immobilization of lions and reported that the duration of immobilization depend on the dose but the onset of immobilization was similar for both low and high dosages

Forsythe *et al* (1992) evaluated the effects of tiletamine zolazepam-xylazine combination with respect to anaesthetic efficacy and potential for tissue damage in Syrian hamsters Two dose levels of the combination were administered by both IP and IM routes The IM route failed to produce anaesthesia consistantly and caused gross and histopathological muscle lesions The IP route produced safe reliable level of surgical anaesthesia without evidence of gross or histopathological lesions There was no nephrotoxicity

Fieni and Tainturier (1993) reported tiletamine zolazepam as a suitable anaesthetic combination for various surgical operations including castration and vasectomy in dogs Its use as anaesthetic for orthopaedic surgery was not recommended because of incomplete muscular relaxation

Ko *et al* (1993) carried out clinical trials with tiletamine-zolazepam mixture in cats and reported that the drug combination provided effective and safe anaesthesia for castration and onichectomy The onset of action was rapid and the induction was smooth Intubation was easy and the muscle relaxation and analgesia were excellent and lasted for 40 minutes Recovery was smooth, with minimal changes in body temperature and cardiorespiratory function

Kristensen and Nielson (1993) employed tiletamine zolazepam alone and in combination with xylazine and butyrophenol for anaesthetizing cats The anaesthesia produced with the administration of tiletamine-zolazepam was unsatisfactory During anaesthesia a significant number of cats had strong muscular contractions and were restless during recovery The anaesthesia produced with the combination of tiletamine-zolazepam, xylazine and butyrophenol was satisfactory

Lin *et al* (1993) evaluated the analgesic and anaesthetic effects of tiletamine zolazepam and tiletamine-zolazepam xylazine combinations in sheep Anaesthesia was characterised by muscle relaxation and profound analgesia with both regimens, but muscle relaxation appeared better and duration of analgesia was significantly longer in sheep which received tiletamine-zolazepam-xylazine combination Significant decrease

in arterial blood pressure was observed at 45 and 60 min after administration of tiletamine-zolazepam-xylazine combination

Fagella *et al* (1994) employed tiletamine-zolazepam for neutering 6 14 week old pups The combination was found unsatisfactory in pups though it provided sufficient anaesthesia to neuter kittens

Lin *et al* (1994) compared the anaesthetic effects of intravenous tiletamine-zolazepam-ketamine (TK) and tiletamine zolazepam ketamine-xylazine (TKX) in sheep after premedication with atropine The duration of analgesia was 28 7 ± 6 9 min with the former and 82 8 ± 26 6 min with the latter Heart rate increased significantly within five minutes after administration in both groups Respiratory rate remained unchanged after TK administration, but increased significantly from five to 45 min after TKX administration Arterial blood pressure decreased significantly at 15 min with TK and 30 min with TKX Sheep remained recumbent for 201 min with TK and 166 min with TKX

Tiwari *et al* (1994) reported that the administration of xylazine with ketamine produced excellent muscle relaxation deep sedation and moderate analgesia with loss of righting reflex in dogs There was increase in blood glucose level but the urea nitrogen, sodium and potassium levels remained unaffected

Materials and Methods

MATERIALS AND METHODS

The experimental study was conducted on 36 apparently healthy adult nondescript dogs of either sex These animals were randomly divided into two groups, viz Group I and II each consisting of 18 animals Group I and II were further divided into three subgroups, viz , A, B and C, consisting of six animals each

All the animals were prepared by withholding food and water for 24 h prior to the experiment Atropine sulphate* at the rate of 0 04 mg/kg bodyweight was administered IM 15 min prior to the administration of the experimental drug(s) in all the animals

The programme of study is given hereunder

Group I

A Tiletamine zolazepam** at the rate of 5 mg/kg bodyweight, was administered IM

B Tiletamine zolazepam at the rate of 10 mg/kg bodyweight, was administered IM

C Tiletamine zolazepam at the rate of 15 mg/kg bodyweight, was administered IM

* Atropine sulphate Rayan Pharma Limited, Anaparty A P

** Zoletil 100 Tiletamine 250 mg and Zolazepam, 250 mg Laboratories Reading, Z A C

Group II

A Xylazine* at the rate 0 5 mg/kg bodyweight and after 15 min tiletamine zolazepam at the rate of 5 mg/kg bodyweight, were administered IM

B Xylazine at the rate 0 5 mg/kg bodyweight and after 15 min tiletamine zolazepam at the rate of 10 mg/kg bodyweight, were administered IM

C Xylazine at the rate 0 5 mg/kg bodyweight and after 15 min tiletamine zolazepam at the rate of 15 mg/kg bodyweight, were administered IM

MAIN ITEMS OF OBSERVATION

I. Clinical observations

1 Clinical signs

The various clinical signs observed following the administration of the drugs were recorded

2 Induction time

It was calculated as the time from injection of Tiletamine zolazepam to the time when the animal assumed lateral recumbency with loss of head righting reflex

*Xylaxin Xylazine hydrochloride 23 22 mg/ml (equivalent to 20 mg of xylazine) Indian Immunologicals Hyderabad

3 Duration of anaesthesia

It was calculated as the time from the assumption of lateral recumbency with loss of headrighting reflex to the return of headrighting reflex

4 Muscle relaxation time

It was calculated as the time from loss of resistance to jaw opening to the return of resistance to jaw opening

5 Degree of muscle relaxation

It was rated as excellent, good, moderate or poor

6 Recovery time

It was calculated as the time from the return of head righting reflex to the time when the animal could stand up and walk unassisted

Laparotomy at the left paralumbar site was performed in two animals of each subgroup of group II 10 min after the administration of tiletamine-zolazepam to assess the anaesthetic effect

II. Physiological observations

Blood samples were collected from the cephalic veins Rectal temperature, pulse rate, respiration rate, systolic and diastolic pressures, and electrocardiogram were recorded immediately before the administration of atropine sulphate and at 15 min 30 min , 60 min and 24 h after the administration of tiletamine zolazepam

Arterial blood pressure (systolic and diastolic)

An inflatable pediatric cuff was fixed on to the fore_imb 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 millimeters of mercury (Harvey *et al* 1983

Coagulation time (whole blood clotting time)

It was recorded employing capillary tube method (Benjamin, 1978) The time interval between the appearance of blood during vein puncture and the appearance of the fibrin strand was calculated as the coagulation time

Electrocardiogram (ECG)

It was recorded using a base apex lead system at a paper speed of 50 mm per second

III. Haemogram

Erythrocyte sedimentation rate (ESR) (Wintrobe 1961) packed cell volume (PCV) (Wintrobe, 1961) haemoglobin concentration using haemoglobin kit* and total erythrocyte count total and differential leukocyte counts (Schalm 1975) were estimated

IV. Serum constituents

Serum glucose value was estimated using Glucose kit** in which GOD/POD method was followed Serum sodium and potassium concentrations were estimated using Atomic Absorption Spectrophotometer (Perkin Elmer Model 2380) Serum chloride concentration was estimated using Chloride kit** based on a modified Schoenfeld and Lewellen's calorimetric method

Total serum protein content was estimated using total protein and albumin kit** by biuret method Serum urea nitrogen level was estimated by Urea kit** by which based on the

* Ortho Diagnostic Systems, Division of Ethnor Limited Bombay
**Stangen Immunodiagnostics Hyderabad

condensation of urea with diacetyl monoxime (DAM) in an acidic medium Aspartate aminotransferase (AST/GOT) value was estimated by SGOT/AST kit* in which Reitman and Frankel's method was followed Alanine aminotransferase (ALT/GPT) was estimated with SGPT (ALT) kit* in which Reitman and Frankel's method was used

V. Post anaesthetic observations

After the experiment, the animals were kept under observation for a period of seven days and post anaesthetic complication if any were recorded

VI. Histopathological examination

Two animals from each subgroups were sacrificed on the eighth day and specimens of liver and kidney were collected and fixed in neutral buffered formalin The fixed tissues were processed and 5 6 um paraffin sections were cut and stained using haematoxylin and eosin (Humason, 1979)

The effects of different doses of tiletamine zolazepam with and without xylazine premedication were assessed by comparing the concerned subgroup means by Students t test (Snedecor and Cochran, 1967)

* Stangen Immunodiagnostics, Hyderabad

Results

RESULTS

GROUP I

The observations are presented in Tables 1 to 9

Subgroup IA

Tiletamine zolazepam combination was administered IM at the rate of 5 mg/kg bodyweight to the animals of this sub group

Clinical observations

The induction time was 6 17 ± 1 01 min the effect persisted for 33 67 ± 5 88 min and the recovery time was 111 50 ± 14 53 min

The animals assumed sternal recumbency by 2 83 ± 0 48 min lateral recumbency with head up position by 4 00 ± 0 52 min and lateral recumbency with loss of headrighting reflex by 6 17 ± 1 01 min Sensitivity to pinprick was sluggish and the loss of headrighting reflex persisted for 33 67 ± 5 88 min

The animals resumed sternal recumbency by 61 67 ± 8 70 min and was able to stand up with incoordination by 8_ 33 ± 13 08 min The gait of the animals became apparently normal b 151 33 ± 12 77 min

The onset of effect was characterised by the winking of eyes followed by yawning, licking and protrusion of tongue Salivation was scanty and the eyes remained open

Palpebral and pedal reflexes were retained Pupils were slightly dilated Swallowing movements were pronounced The jaw muscles maintained the tonus

The respiration was thoraco-abdominal, shallow and regular The relaxation of the abdominal muscles and limbs was moderate

During recovery paddling and vocalization were noticed in some animals All the animals resumed feeding and drinking soon after recovery

Physiological observations

The rectal temperature (°C) was 38 83 ± 0 14 before administration 38 80 ± 0 11 at 15 min, 38 39 ± 0 20 at 30 min 38 39 ± 0 28 at 6 min and 38 82 ± 0 13 at 24 h The variations were marginal

The pulse rate (per min) was 99 67 ± 5 62 before administration 152 83 ± 7 08 at 15 min 145 00 ± 15 73 at 30 min 142 33 ± 14 72 at 60 min and 95 33 ± 3 85 at 24 h There was significant ($P<0.05$) increase in pulse rate at 15 min 30 min and 60 min which became normal by 24 h

The respiration rate (per min) was 32 50 ± 4 39 before administration 23 33 ± 1 52 at 15 min, 27 83 ± 1 47 at 30 min 32 00 ± 3 83 at 60 min and 31 33 ± 4 64 at 24 h There was decrease in respiration rate though not significant at 15 min and 30 min, became normal by 60 min

The systolic pressure (mm Hg) was 147 35 ± 5 4 before administration 146 00 ± 5 19 at 15 min, 144 33 ± 5 20 at 30 min 147 00 ± 6 55 at 60 min and 148 67 ± 6 63 at 24 h The variations were marginal

The diastolic pressure (mm Hg) was 88 33 ± 3 1- before administration 92 67 ± 1 61 at 15 min 90 50 ± 1 93 at 30 min 95 00 ± 1 84 at 60 min and 97 00 ± 5 38 at 24 h There was increase in diastolic pressure, though not significant

The coagulation time (min) of blood was 3 3- ± 0 5- before administration, 3 75 ± 0 38 at 15 min 3 42 ± 0 30 at 30 min 2 83 ± 0 40 at 60 min and 3 33 ± 0 25 at 24 h The variations were marginal

Electrocardiogram (ECG)

Increase in heart rate was noticed in all the animals at 15 min after the administration of tiletamine-zolazepam and persisted upto 60 min Depression of T wave was noticed in two animals at 15 min and in one animal it persisted at 30 min also

Spiking of T wave was noticed in one animal at 15 min and 30 min All the ECG changes were seen spontaneously corrected by 24 h (Fig 1)

Haemogram

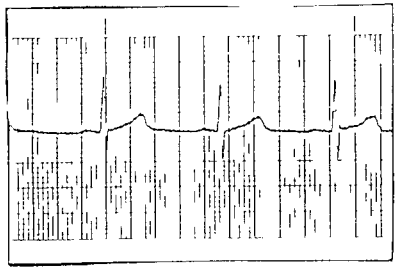
The erythrocyte sedimentation rate (mm/1 h) was 2 00 ± 0 26 before administration 1 50 ± 0 22 at 15 min 1 3 ± 0 2_ at 30 min, 1 17 ± 0 17 at 60 min and 1 6" ± 0 21 at 24 h Gradual decrease in ESR was noticed following the administration of the drug, and the decrease at 60 min was significant (P<0 05)

The packed cell volume (per cent) was 37 00 ± 2 -_ before administration 34 83 ± 1 74 at 15 min 32 50 ± 1 12 at 30 min 33 83 ± 1 99 at 60 min and 34 50 ± 2 43 at 24 h There was reduction in the PCV

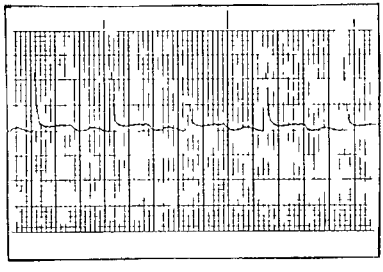
The haemoglobin concentration (g/dl was 11 83 ± 0 oo before administration 11 66 ± 0 63 at 15 min 12 55 ± 0 67 at 30 min 11 44 ± 0 81 at 60 min and 10 99 ± 1 21 at 24 h The variations were marginal

The total erythrocyte count (10° mm) was 4 72 ± 0 43 before administration 4 67 ± 0 39 at 15 min 3 72 ± 0 41 at 30 min 4 97 ± 0 41 at 60 min and 4 95 ± 0 18 at 24 h There was decrease in TEC upto 30 min and thereafter an increase

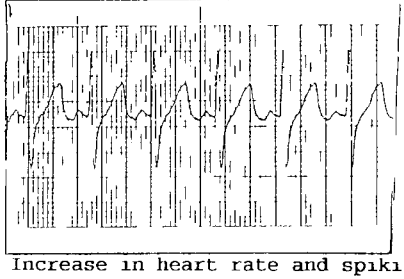
Fig 1 ECG changes following the administration of tiletamine zolazepam (5 mg/kg bodyweight) in dogs (Subgroup IA)



A Normal



B Depression of T wave



C Increase in heart rate and spiking of T-wave

The total leukocyte count ($10^3/mm^3$) was 8 75 ± 0 84 before administration 10 38 ± 0 87 at 15 min, 10 40 ± 0 84 at 30 min, 10 30 ± 1 21 at 60 min and 10 88 ± 1 07 at 24 h There was increase in TLC, though not significant

The neutrophil count (per cent) was 67 83 ± 2 82 before administration 68 17 ± 1 60 at 15 min, 65 33 ± 2 70 at 30 min 62 50 ± 3 90 at 60 min and 64 17 ± 2 12 at 24 h There was increase in neutrophil count at 15 min and thereafter a decrease

The lymphocyte count (per cent) was 23 33 ± 2 44 before administration 21 00 ± 2 95 at 15 min 21 50 ± 2 67 at 30 min 24 00 ± 3 02 at 60 min and 23 17 ± 2 24 at 24 h There was decrease in lymphocyte count at 15 min and an increase thereafter which reached near normal value by 24 h

The monocyte count (per cent) was 4 33 ± 2 38 before administration - 33 ± 0 67 at 15 min 6 17 ± 0 95 at 30 min 7 67 ± 1 94 at 60 min and 8 00 ± 1 88 at 24 h There was increase in monocyte count from 30 min onwards and the increase persisted even at 24 h

The eosinophil count (per cent) was 4 33 ± 1 52 before administration 33 ± 1 50 at 15 min 7 00 ± 2 42 at 30 min 5 50 - 1 45 at 60 min and 4 67 ± 1 02 at 24 h There was

increase in eosinophil count at 15 min and 30 min and thereafter it was decreased to near normal value by 24 h

The basophil count (per cent) was insignificant

Serum constituents

The serum glucose value (mg/dl) was 84 72 ± 15 53 before administration 108 14 ± 11 68 at 15 min 116 07 ± 12 70 at 30 min 135 89 ± 15 60 at 60 min and 116 32 ± 14 00 at 24 h There was gradual increase in glucose value upto 60 min and the increase was significant (P<0 05) at 60 min

The serum sodium concentration (mEq/L) was 104 90 ± 6 43 before administration, 103 27 ± 9 45 at 15 min 110 70 ± 14 95 at 30 min 105 26 ± 13 51 at 60 min and 100 55 ± 8 28 at 24 h The variations were marginal

The serum potassium concentration (mEq/L) was 4 98 ± 0 17 before administration, 5 17 ± 0 17 at 15 min, 5 11 ± 0 27 at 30 min 5 36 ± 0 32 at 60 min and 5 45 ± 0 35 at 24 h The variations were marginal

The serum chloride concentration mEq/L) was 104 60 ± 7 33 before administration 117 33 ± 6 24 at 15 min 113 61 ± 9 02 at 30 min 121 31 ± 5 59 at 60 min and 102 44 ± 6 73 at 24 h There was increase in serum chloride concentration at 15 min 30 min and 60 min and became normal by 24 h

The total serum protein content (g/dl) was 5 53 ± 0 49 before administration 4 75 ± 0 34 at 15 min 5 10 ± 0 41 at 30 min 5 10 ± 0 38 at 60 min and 5 83 ± 0 65 at 24 h The variations were marginal

The serum urea nitrogen value (mg/dl) was 12 54 ± 2 86 before administration 13 46 ± 2 47 at 15 min, 10 16 ± 1 52 at 30 min 12 27 ± 2 18 at 60 min and 10 50 ± 2 05 at 24 h Only marginal variations were noticed in the serum urea nitrogen value

The serum aspartate aminotransferase (AST) value (units/ml) was 39 17 ± 6 54 before administration 43 75 ± 10 12 at 15 min, 51 67 ± 11 59 at 30 min, 54 58 ± 13 60 at 60 min and 54 17 ± 15 42 at 24 h There was gradual increase in AST value but the increase was not significant

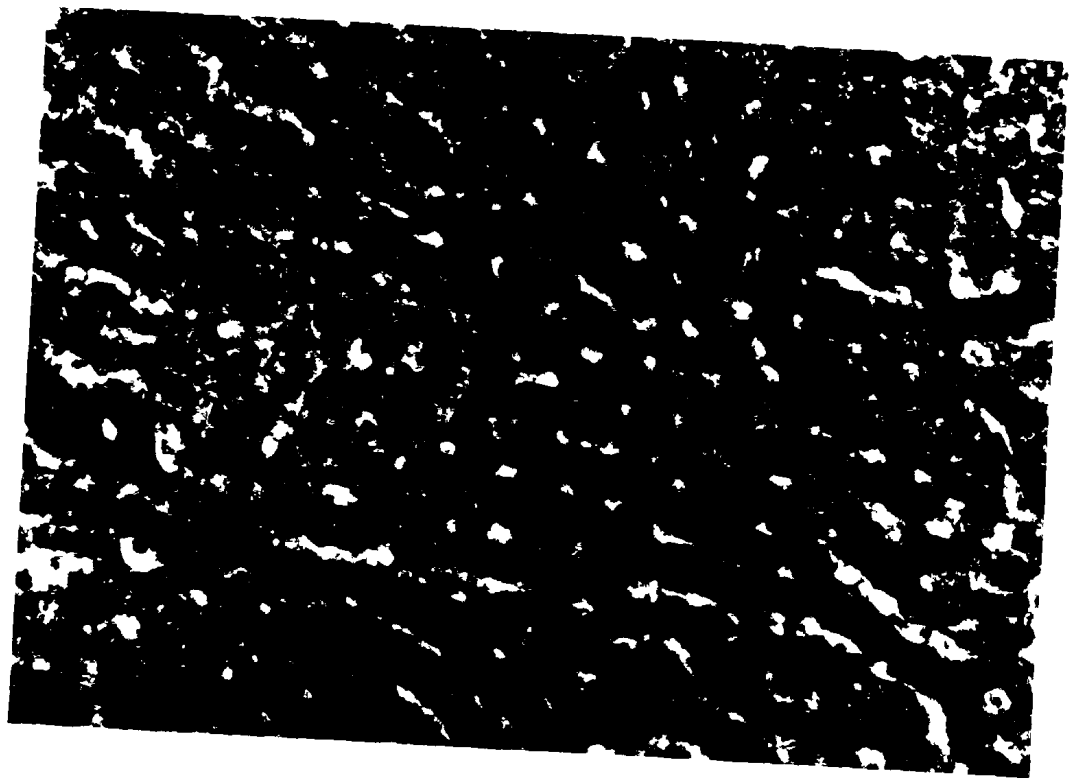
The serum alanine aminotransferase (ALT) value (units/ml) was 29 33 ± 5 55 before administration, 29 67 ± 5 20 at 15 min 34 67 ± 6 10 at 30 min, 37 00 ± 2 95 at 60 min and 37 00 ± 5 05 at 24 h There was gradual increase in ALT value but the increase was not significant

Histopathological examination

Histopathological examination revealed mild fatty changes in liver Fig 2) and a few dilated tubules along with focal areas of necrosis in kidney (Fig 3)

Fig 2 Photomicrograph of the liver showing fatty changes(A) (Subgroup IA) H&E x 250

Fig 3 Photomicrograph of the kidney showing dilated tubules(4) along with focal areas of nephrosis(3)(Subgroup IA) H&E x 250



Subgroup IB

Tiletamine-zolazepam combination was administered IM at the rate of 10 mg/kg bodyweight to the animals of this sub-group

Clinical observations

All the animals evinced pain during the administration of tiletamine-zolazepam The induction time was 4 33 ± 0 21 min, the effect persisted for 57 83 ± 6 17 min and the recovery time was 116 50 ± 10 46 min

The animals assumed sternal recumbency by 1 67 ± 0 21 min lateral recumbency with head up position by 3 00 ± 0 26 min and lateral recumbency with loss of headrighting reflex by 4 33 ± 0 21 min Sensitivity to pinprick was sluggish and the loss of headrighting reflex persisted for 57 83 ± 6 17 min

The animals resumed sternal recumbency by 90 50 ± 12 27 min and was able to stand up with incoordination by 117 17 ± 8 47 min The gait of the animals became apparently normal by 178 67 ± 14 41 min

The onset of effect was characterised by the winking of eyes followed by yawning licking and protrusion of tongue Salivation was scanty and the eyes remained open throughout

Palpebral and pedal reflexes were retained Pupils were dilated Swallowing movements were pronounced during the induction period thereafter it was occasional The jaw muscles maintained the tonus

The respiration was thoraco-abdominal in three animals and in others it was abdominal, but was regular in all animals In those with abdominal respiration the relaxation of the abdominal muscles and limbs was good and in others it was moderate

During recovery paddling and vocalization were noticed in some animals All the animals resumed feeding and drinking soon after recovery

Physiological observations

The rectal temperature (°C) was 39 30 ± 0 11 before administration, 39 02 ± 0 18 at 15 min 38 28 ± 0 29 at 30 min 37 99 ± 0 30 at 60 min and 38 93 ± 0 15 at 24 h There was significant ($P<0.05$) decrease in rectal temperature at 30 min and 60 min which became normal by 24 h

The pulse rate (per min) was 107 33 ± 11 75 before administration 159 50 ± 9 22 at 15 min 169 83 ± 10 68 at 30 min 132 67 ± 10 83 at 60 min and 98 00 ± 7 69 at 24 h There was significant ($P<0.05$) increase in pulse rate at 15 min and 30 min and thereafter decreased to near normal value by 24 h

The respiration rate (per min) was 39 67 ± 8 54 before administration, 23 17 ± 3 71 at 15 min, 26 83 ± 3 94 at 30 min 30 50 ± 3 73 at 60 min and 33 50 ± 3 70 at 24 h There was decrease in respiration rate at 15 min and then gradually increased towards the base line value

The systolic pressure (mm Hg) was 148 33 ± 2 60 before administration 144 33 ± 4 33 at 15 min, 142 33 ± 7 44 at 30 min 147 33 ± 5 62 at 60 min and 150 33 ± 6 54 at 24 h The variations were not significant

The diastolic pressure (mm Hg) was 87 33 ± 3 17 before administration 88 33 ± 6 74 at 15 min, 83 67 ± 4 72 at 30 min 90 00 ± 2 13 at 60 min and 88 00 ± 3 54 at 24 h The variations were not significant

The coagulation time (min) of blood was 3 58 ± 0 45 before administration 4 25 ± 0 28 at 15 min 4 17 ± 0 42 at 30 min 3 67 ± 0 33 at 60 min and 3 75 ± 0 31 at 24 h The variations were marginal

Electrocardiogram (ECG)

Increase in heart rate was noticed in all the animals at 15 min after the administration of tiletamine-zolazepam and persisted upto 60 min except in one animal in which it was seen slightly reduced by 60 min Biphasic T-wave was noticed in one animal at 15 min and 30 min but at 24 h there was slight

reduction in heart rate and increase in amplitude of R wave along with biphasic T wave Increase in amplitude of R wave was noticed in one animal at 15 min, thereafter it became normal Depression of T wave was noticed in one animal at 30 min and 60 min and became normal by 24 h All the ECG changes were spontaneously corrected by 24 h except in one animal (Fig 4)

Haemogram

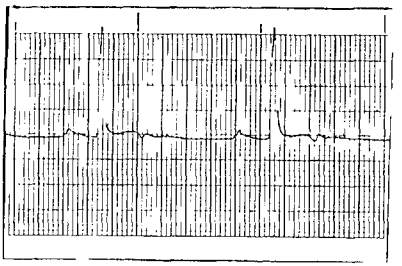
The erythrocyte sedimentation rate (mm/1 h) was 2 00 ± 0 26 before administration, 2 33 ± 0 21 at 15 min 2 00 ± 0 36 at 30 min, 1 67 ± 0 33 at 60 min and 1 67 ± 0 21 at 24 h There was increase in ESR at 15 min and thereafter there was gradual decrease

The packed cell volume (per cent) was 37 00 ± 2 41 before administration, 37 17 ± 1 60 at 15 min 38 17 ± 1 99 at 30 min, 36 50 ± 84 at 60 min and 37 00 ± 1 77 at 24 h There was gradual reduction in PCV

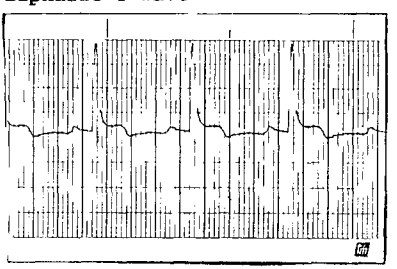
The haemoglobin concentration (g/dl) was 10 54 ± 1 03 before administration 10 43 ± 0 72 at 15 min, 10 77 ± 0 92 at 30 min, 11 43 ± 71 at 60 min and 10 38 ± 1 17 at 24 h The variations were marginal

The total erythrocyte count ($10^6/mm^3$) was 4 50 ± 0 48 before administration 4 05 ± 0 30 at 15 min 4 57 ± 0 14 at

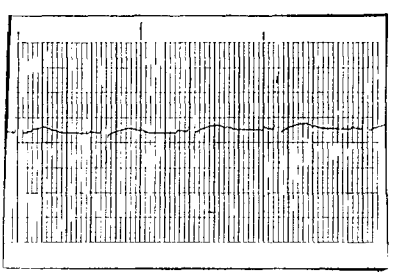
Fig 4 ECG changes following the administration of tiletamine zolazepam (10 mg/kg bodyweight) in dogs (Subgroup IB)



A Biphasic T-wave



B Increase in R wave amplitude



C Depression of T wave

30 min, 4 78 ± 0 27 at 60 min and 4 98 ± 0 45 at 24 h There was decrease in TEC at 15 min and thereafter a gradual increase

The total leukocyte count (10^3/mm) was 12 13 ± 1 10 before administration, 12 28 ± 1 51 at 15 min 12 43 ± 2 13 at 30 min 12 82 ± 3 55 at 60 min and 10 83 ± 1 02 at 24 h There was gradual increase in TLC and the count was seen decreased at 24 h

The neutrophil count (per cent) was 71 17 ± 2 18 before administration 67 50 ± 2 43 at 15 min 64 67 ± 2 39 at 30 min 64 83 ± 2 24 at 60 min and 68 00 ± 3 11 at 24 h There was decrease in neutrophil count, upto 60 min

The lymphocyte count (per cent) was 21 83 ± 1 54 before administration 21 33 ± 2 04 at 15 min 22 33 ± 1 69 at 30 min 21 83 ± 1 58 at 60 min and 23 17 ± 2 24 at 24 h Slight increase in the count was observed at 24 h

The monocyte count (per cent) was 4 33 ± 0 80 before administration 6 33 ± 2 12 at 15 min, 6 67 ± 1 41 at 30 min 6 67 ± 1 36 at 60 min and 5 83 ± 1 14 at 24 h There was increase in monocyte count

The eosinophil count (per cent) was 2 17 ± 0 48 before administration 4 50 ± 0 56 at 15 min 4 83 ± 1 33 at 30 min 4 50 ± 1 48 at 60 min and 4 17 ± 1 22 at 24 h There was

increase in eosinophil count and the increase at 15 min was significant (P<0 05)

The basophil count (per cent) was insignificant

Serum constituents

The serum glucose value (mg/dl) was 85 12 ± 10 37 before administration 99 41 ± 12 11 at 15 min 103 57 ± 6 05 at 30 min 132 14 ± 3 06 at 60 min and 98 81 ± 14 74 at 24 h There was gradual increase in glucose value upto 60 min and the increase at 60 min was significant (P<0 05)

The serum sodium concentration (mEq/L) was 126 11 ± 10 85 before administration 107 08 ± 3 48 at 15 min 119 77 ± 11 85 at 30 min 107 23 ± 4 62 at 60 min and 110 89 ± 5 36 at 24 h There was decrease in serum sodium concentration following the administration of the drugs

The serum potassium concentration (mEq/L) was 5 22 ± 0 16 before administration, 4 86 ± 0 09 at 15 min, 5 18 ± 0 25 at 30 min, 5 22 ± 0 28 at 60 min and 5 28 ± 0 24 at 24 h The variations were marginal

The serum chloride concentration (mEq/L) was 107 51 ± 5 23 before administration 121 86 ± 5 44 at 15 min 118 24 ± 6 13 at 30 min 115 40 ± 7 13 at 60 min and 123 72 ± 6 75 at

Histopathological examination

Histopathological examination revealed cloudy swelling (Fig 5) and fatty changes in liver and cystic dilation of tubules along with focal areas of nephrosis in kidney

Subgroup IC

Tiletamine-zolazepam combination was administered IM at the rate of 15 mg/kg bodyweight to the animals of this sub-group

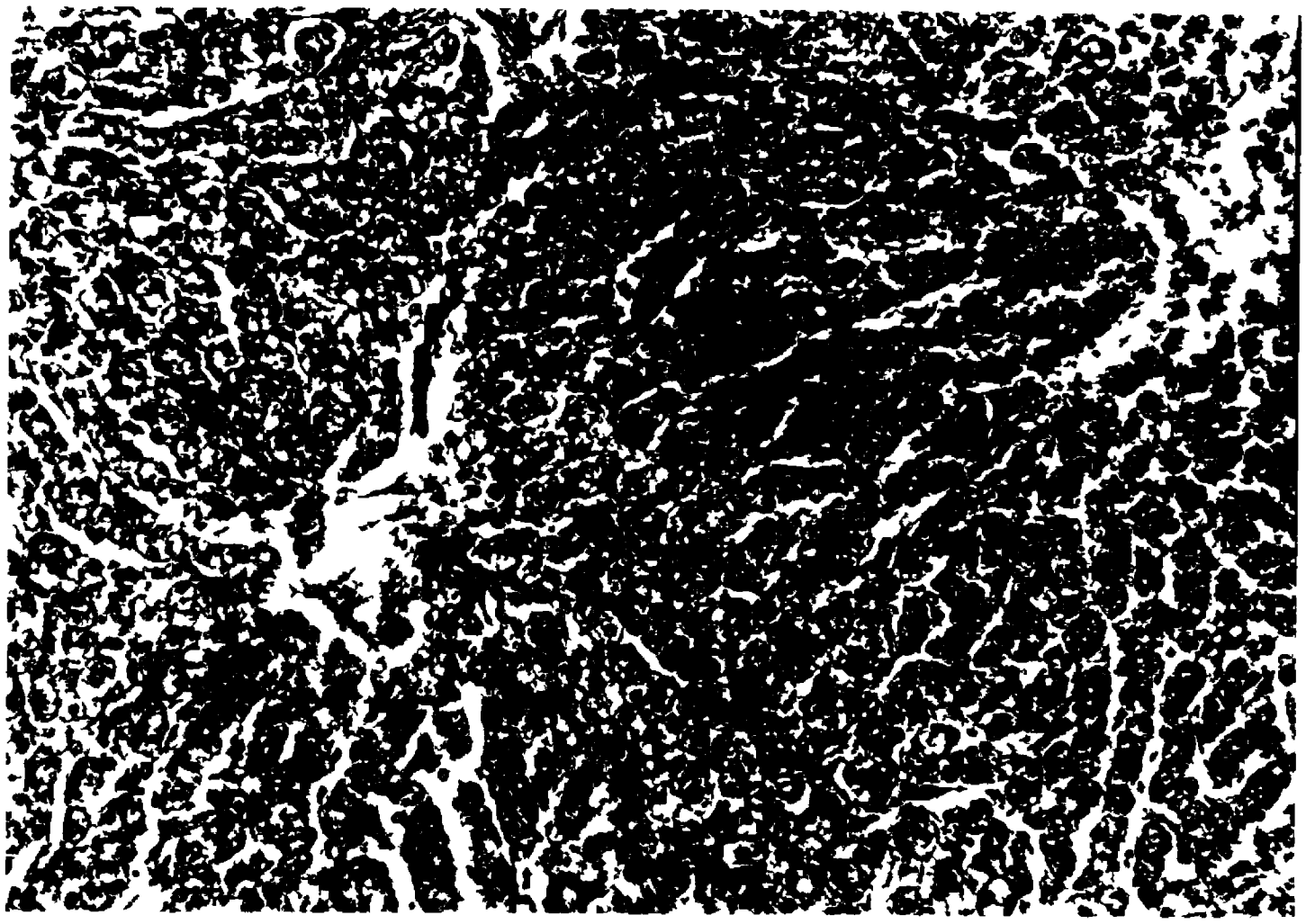
Clinical observations

All the animals evinced pain during the administration of tiletamine-zolazepam The induction time was 4 33 ± 0 49 min the effect persisted for 89 00 ± 20 86 min and the recovery time was 180 33 ± 10 57 min

The animals assumed sternal recumbency by 1 67 ± 0 21 min lateral recumbency with head up position by 2 83 ± 0 31 min and lateral recumbency with loss of headrighting reflex by 4 33 ± 0 49 min Sensitivity to pinprick was sluggish and the loss of headrighting reflex persisted for 89 00 ± 20 86 min

The animals resumed sternal recumbency by 138 83 ± 17 32 min and was able to stand up with incoordination by

Fig 5 Photomicrograph of the liver showing cloudy swelling (Subgroup IB) H&E x 250



195 67 ± 15 15 min The gait of the animals became apparently normal by 273 67 ± 19 80 min

The onset of effect was characterised by the winking of eyes followed by yawning, licking and protrusion of tongue Salivation was scanty and the eyes remained open throughout

Palpebral and pedal reflexes were retained Pupils were slightly dilated Swallowing movements were prorounced during induction period and thereafter it was occasional The jaw muscles, though not fully relaxed, permitted easy manipulation for endotracheal intubation

The respiration was abdominal and regular in all the animals The relaxation of the abdominal muscles and limbs was good

During recovery paddling and vocalization were not a common feature in all the animals All the animals resumed feeding and drinking soon after recovery

Physiological observations

The rectal temperature (°C) was 39 11 ± 0 11 before administration 38 87 ± 0 24 at 15 min 38 09 ± 0 33 at 30 min 37 93 ± 0 35 at 60 min and 38 87 ± 0 13 at 24 h There was significant ($P<0.05$) decrease in rectal temperature at 30 min and 60 min which became normal by 24 h

The pulse rate (per min) was 117 50 ± 9 17 before administration 140 33 ± 13 31 at 15 min 142 67 ± 14 73 at 30 min 120 00 ± 14 30 at 60 min and 120 00 ± 8 18 at 24 h There was increase in pulse rate at 15 min and 30 min which reached near normal value by 60 min

The respiration rate (per min) was 38 17± 5 00 before administration 26 00 ± 4 51 at 15 min 25 83 ± 2 59 at 30 min 33 83 ± 3 99 at 60 min and 36 83 ± 4 76 at 24 h There was decrease in respiration rate at 15 min and 30 min but was not significant and thereafter it increased towards the base line value

The systolic pressure (mm Hg) was 142 33 ± 4 18 before administration 142 00 ± 4 41 at 15 min, 142 67 ± 5 28 at 30 min 141 67 ± 5 38 at 60 min and 141 00 ± 4 31 at 24 h The variations were marginal

The diastolic pressure (mm Hg) was 87 00 ± 1 24 before administration 88 33 ± 2 94 at 15 min, 87 33 ± 3 04 at 30 min 86 33 ± 1 50 at 60 min and 90 67 ± 2 56 at 24 h After a slight initial increase at 15 min the diastolic pressure decreased to the base line value at 30 min

The coagulation time (min) of blood was 4 25 ± 0 25 before administration 3 58 ± 0 35 at 15 min 4 08 ± 0 35 at

30 min 3 92 ± 0 45 at 60 min and 4 25 ± 0 38 at 24 h The variations were marginal

Electrocardiogram (ECG)

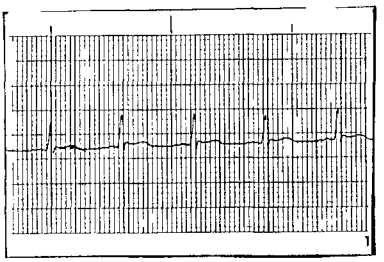
Increase in heart rate was noticed in all the animals at 15 min after the administration of tiletamine zolazepam and became normal at 60 min in two animals Depression of T wave and QRS complex was noticed in one animal at 15 min and 30 min At 60 min there was biphasic T-wave along with T wave depression and it became normal by 24 h Increase in T wave period with bifid T-wave at the apex was noticed in one animal but it became normal by 24 h Biphasic T wave was noticed in one animal at 60 min, and at 24 h there was inversion of T wave along with biphasic T-wave Spiking of T wave along with biphasic P wave was noticed in one animal at 60 min but became normal by 24 h The heart rate became normal/slightly reduced by 24 h (Fig 6)

Haemogram

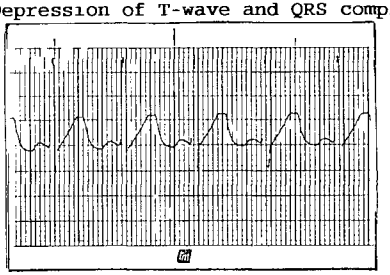
The erythrocyte sedimentation rate (mm/1 h) was 2 00 ± 0 26 before administration 1 50 ± 0 34 at 15 min 1 67 ± 0 42 at 30 min 1 33 ± 0 21 at 60 min and 1 33 ± 0 21 at 24 h There was decrease in ESR but was not significant

The packed cell volume (per cent) was 37 33 ± 0 67 before administration 36 50 ± 1 41 at 15 min 35 50 ± 1 28 at

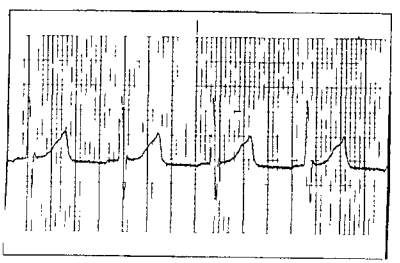
Fig 6 ECG changes following the administration of tiletamine zolazepam (15mg/kg bodyweight) in dogs (Subgroup IC)



A Depression of T-wave and QRS complex



B Increase in T-period with bifid T-wave at the apex



C Spiking of T wave and biphasic P-wave

30 min 35 17 ± 0 95 at 60 min and 35 83 ± 2 39 at 24 h There was gradual reduction in PCV, but was not significant

The haemoglobin concentration (g/dl) was 13 00 ± 0 90 before administration 11 32 ± 1 42 at 15 min 11 16 ± 1 46 at 30 min, 11 16 ± 1 11 at 60 min and 11 49 ± 0 78 at 24 h There was gradual decrease in haemoglobin concentration though not significant

The total erythrocyte count ($10^6/mm^3$) was 5 82 ± 0 59 before administration 4 95 ± 0 28 at 15 min, 4 53 ± 0 52 at 30 min 4 42 ± 0 38 at 60 min and 5 92 ± 0 67 at 24 h There was gradual decreases in TEC upto 60 min but reached near normal value by 24 h

The total leukocyte count ($10^3/mm^3$) was 9 43 ± 0 68 before administration 8 72 ± 0 48 at 15 min 5 98 ± 1 21 at 30 min, 8 30 ± 0 63 at 60 min and 8 42 ± 0 88 at 24 h There was decrease in TLC and the decrease was significant ($P<0\ 05$) at 30 min

The neutrophil count (per cent) was 71 50 ± 2 79 before administration 69 00 ± 2 27 at 15 min 68 00 ± 1 67 at 30 min 69 00 ± 1 90 at 60 min and 69 50 ± 0 50 at 24 h There was decrease in neutrophil count throughout the period of observation

The lymphocyte count (per cent) was 18 33 ± 1 76 before administration 21 17 ± 1 56 at 15 min, 20 67 ± 1 05 at 30 min 22 00 ± 1 90 at 60 min and 22 17 ± 0 93 at 24 h There was increase in lymphocyte count

The monocyte count (per cent) was 3 67 ± 1 58 before administration 6 00 ± 1 63 at 15 min, 7 00 ± 1 75 at 30 min 6 17 ± 1 33 at 60 min and 5 17 ± 1 08 at 24 h There was increase in monocyte count

The eosinophil count (per cent) was 5 17 ± 1 45 before administration 3 67 ± 2 12 at 15 min, 4 33 ± 1 12 at 30 min 3 17 ± 1 30 at 60 min and 4 17 ± 0 79 at 24 h There was decrease in eosinophil count

The basophil count (per cent) was insignificant

Serum constituents

The serum glucose value (mg/dl) was 101 73 ± 8 99 before administration 118 35 ± 12 41 at 15 min, 119 19 ± 13 35 at 30 min 100 51 ± 12 46 at 60 min and 111 01 ± 13 08 at 24 h There was increase in the value at 15 min and 30 min but was not significant and reached near normal value by 60 min

The serum sodium concentration (mEq/L) was 114 68 ± 13 36 before administration 112 51 ± 2 44 at 15 min 108 27 ± 7 29 at 30 min 115 41 ± 15 91 at 60 min and 123 50 ± 8 92 at

24 h There was decrease in serum sodium concentration upto 30 min but thereafter it increased above base line value

The serum potassium concentration (mEq/L) was 5 70 ± 0 27 before administration 5 36 ± 0 38 at 15 min 5 86 ± 0 20 at 30 min 5 70 ± 0 28 at 60 min and 5 49 ± 0 14 at 24 h The variations were marginal

The serum chloride concentration (mEq/L) was 107 83 ± 7 91 before administration, 103 37 ± 6 60 at 15 min 110 85 ± 7 60 at 30 min 118 41 ± 9 55 at 60 min and 102 99 ± 9 32 at 24 h After an initial decrease in serum chloride concentration at 15 min it increased at 30 min and 60 min and then decreased but changes were not significant

The total serum protein content (g/dl) was 5 56 ± 0 34 before administration 6 00 ± 0 48 at 15 min 5 48 ± 0 21 at 30 min 6 18 ± 0 45 at 60 min and 5 65 ± 0 56 at 24 h The variations were marginal

The serum urea nitrogen value (mg/dl) was 9 60 ± 1 60 before administration 11 02 ± 2 44 at 15 min, 10 98 ± 1 83 at 30 min 10 62 ± 1 93 at 60 min and 11 14 ± 2 01 at 24 h Only marginal variations were noticed in the serum urea nitrogen value

The serum aspartate aminotransferase (AST) value (units/ml) was 29 17 ± 7 26 before administration 34 58 ± 11 24 at 15 min, 30 00 ± 7 44 at 30 min, 40 50 ± 8 21 at 60 min and 41 25 ± 13 67 at 24 h There was increase in AST value but was not significant

The serum alanine aminotransferase (ALT) value (units/ml) was 29 00 ± 4 55 before administration 29 33 ± 3 04 at 15 min, 30 67 ± 4 37 at 30 min, 27 67 ± 5 87 at 60 min and 34 67 ± 6 72 at 24 h The variations were marginal upto 60 min but an increase in value was observed at 24 h

Histopathological examination

Histopathological examination revealed cloudy swelling and mild fatty changes in liver and cystic dilation of tubules along with focal areas of nephrosis in kidney

Table 1 The induction time recovery time duration of analgesia and duration of effect following the administration of tiletamine-zolazepam (Group I) and with xylazine premedication (Group II) in dogs (Time in minutes) (Mean + SE)

n 6

	Group I			Group II		
	A	B	C	A	B	C
Assumption of sternal recumbency	2 83+ 0 48	1 67+ 0 21	1 67+ 0 21	1 83+ 0 40	1 33+ 0 21	1 33+ 0 21
Assumption of lateral recumbency with head up	4 00+ 0 52	3 00+ 0 26	2 83± 0 31			-
Assumption of lateral recumbency with loss of headrighting reflex	6 17± 1 01	4 33+ 0 21	4 33± 0 49	3 33+ 0 62	3 17± 0 48	2 83+ 0 54
Loss of sensitivity to pinprick	-			6 00+ 1 16	5 17+ 0 70	5 00+ 0 37
Return of sensitivity to pinprick	-	-	-	35 00+ 2 86	61 67+ 5 73	67 50+ 9 60
Return of headrighting reflex	39 83+ 5 93	62 17± 6 18	93 33+ 20 94	53 00+ 6 06	108 33± 10 22	128 67+ 10 65
Resumption of sternal recumbency	61 67+ 8 70	90 50+ 12 27	138 83+ 17 32	64 83± 7 03	157 50+ 28 42	158 33+ 10 99
Could stand up with incoordination	81 33+ 13 08	117 17+ 8 47	195 67± 15 15	101 17+ 10 52	182 83+ 27 99	201 17+ 9 19
Normal gait	151 33+ 12 77	178 67+ 14 41	2 3 67+ 19 80	213 00+ 16 84	288 33+ 19 13	309 67+ 12 86
Induction time	6 17+ 1 01	4 33± 0 21	4 33± 0 49	3 33± 0 62	3 17± 0 48	2 83+ 0 54
Duration of analgesia				29 00+ 3 37	59 83+ 6 40	65 83+ 9 86
Duration of lateral recumbency with loss of headrighting reflex	33 67+ 5 88	57 83+ 6 17	89 00+ 20 86	49 67+ 6 43	105 17+ 10 31	125 83+ 0 8
Recovery time	111 50+ 14 53	1 6 50+ 10 46	190 33+ 0 57	160 00+ 1 70	180 00+ 14 94	181 00+ 12 82

Table 2. Effect of administration of tiletamine-zolazepam on rectal temperature, pulse rate and respiration rate in dogs (Group I) (Mean + SE)

n=6

	Sub-group	0 Min.	15 Min.	30 Min.	60 Min.	24 h
Rectal temperature (°C)	A	38.83+0.14	38.80+0.11	38.39+0.20	38.39±0.28	38.82±0.13
	B	39.30±0.11	39.02±0.18	38.28±0.29 *	37.99±0.30 *	38.93±0.15
	C	39.11+0.11	38.87±0.24	38.09+0.33	37.93±0.35	38.87±0.13
Pulse rate (per min)	A	99.67±5.62	152.83±7.08 *	145.00±15.73 *	142.33±16.72 *	95.33 ±3.85
	B	107.33±11.75	159.50±9.22 *	169.83±10.68 *	132.67±10.83	98.00 ±7.69
	C	117.50±9.17	140.33±13.31	142.67±14.73	120.00±14.30	120.00±8.18
Respiration rate (per min)	A	32.50±4.39	23.33±1.52	27.83±1.47	32.00±3.83	31.33±4.64
	B	39.67±8.54	23.17±3.71	26.83±3.94	30.50±3.73	33.50±3.70
	C	38.17+5.00	26.00+4.51	25.83+2.59	33.83+3.99	36.83±4.76

* Significant at 5 per cent level as compared to the value at 0 min.

Table 3. Effect of administration of tiletamine-zolazepam on systolic pressure, diastolic pressure and coagulation time of blood in dogs (Group I) (Mean ± SE)

n=6

	Sub-group	0 Min.	15 Min.	30 Min.	60 Min.	24 h
Systolic pressure (mm Hg)	A	147.33+5.43	146.00+5.19	144.33+5.10	147.00+6.55	148.67±6.63
	B	148.33±2.60	144.33±4.33	142.33±7.44	147.33±5.62	150.33±6.54
	C	142.33±4.18	142.00±4.41	142.67±5.28	141.67±5.38	141.00±4.31
Diastolic pressure (mm Hg)	A	88.33±3.16	92.67±1.61	90.50±1.93	95.00±1.84	97.00±5.38
	B	87.33±3.17	88.33±6.74	83.67±4.72	90.00±2.13	88.00±3.54
	C	87.00±1.24	88.33±2.94	87.33±3.04	86.33±1.50	90.67±2.56
Coagulation time of blood (in min)	A	3.33±0.54	3.75±0.38	3.42±0.30	2.83±0.40	3.33±0.25
	B	3.58±0.45	4.25±0.28	4.17±0.42	3.67±0.33	3.75±0.31
	C	4.25±0.25	3.58±0.35	4.08±0.35	3.92+0.45	4.25±0.38

Table 4. Effect of administration of tiletamine-zolazepam on erythrocyte sedimentation rate, packed cell volume and haemoglobin concentration in dogs (Group I) (Mean ± SE)

n=6

	Sub-group	0 Min.	15 Min.	30 Min.	60 Min.	24 h
Erythrocyte sedimentation rate (mm/1 h)	A	2.00+0.26	1.50±0.22	1.33±0.21	1.17±0.17*	1.67±0.21
	B	2.00±0.26	2.33±0.21	2.00±0.36	1.67+0.33	1.67±0.21
	C	2.00±0.26	1.50+0.34	1.67±0.42	1.33±0.21	1.33±0.21
Packed cell volume (per cent)	A	37.00±2.41	34.83±1.74	32.50±1.12	33.83±1.99	34.50±2.43
	B	37.17±2.20	37.17±1.60	38.17±1.99	36.50±1.84	37.00±1.77
	C	37.33±0.67	36.50±1.41	35.50±1.28	35.17±0.95	35.83±2.39
Haemoglobin concentration (g/dl)	A	11.83±0.66	11.66±0.63	12.55±0.67	11.44±0.81	10.99±1.21
	B	10.54+1.03	10.43±0.72	10.77+0.92	11.43+0.71	10.38±1.17
	C	13.00+0.90	11.32±1.42	11.16±1.46	11.16+1.11	11.49±0.78

* Significant at 5 per cent level as compared to the value at 0 min.

Table 5 Effect of administration of tiletamine - zolazepam on total erythrocyte, total leukocyte and neutrophil counts in dogs (Group I) (Mean ± SE)

n=6

	Sub-group	0 Min.	15 Min.	30 Min.	60 Min.	24 h
Total erythrocyte count ($10^6/mm^3$)	A	4.72+0.43	4.67+0.39	3.72+0.41	4.97±0.41	4.95±0.18
	B	4.50±0.48	4.05±0.30	4.57±0.14	4.78±0.27	4.98±0.45
	C	5.82±0.59	4.95±0.28	4.53±0.52	4.42±0.38	5.92±0.67
Total leukocyte count ($10^3/mm^3$)	A	8.75±0.84	10.38±0.87	10.40±0.84	10.30±1.21	10.88±1.07
	B	12.13±1.10	12.28±1.51	12.43±2.13	12.82±3.55	10.83±1.02
	C	9.43±0.68	8.72±0.48	5.98±1.21 *	8.30±0.63	8.42±0.88
Neutrophil count (per cent)	A	67.83±2.82	68.17±1.60	65.33±2.70	62.50±3.90	64.17±2.12
	B	71.17±2.18	67.50±2.43	64.67±2.39	64.83+2.24	68.00±3.11
	C	71.50±2.79	69.00+2.27	68.00±1.67	69.00+1.90	69.50+0.50

* Significant at 5 per cent level as compared to the value at 0 min.

Table 6. Effect of administration of tiletamine-zolazepam on lymphocyte, monocyte and eosinophil counts in dogs (Group I) (Mean ± SE)

n=6

	Sub-group	0 Min.	15 Min.	30 Min.	60 Min.	24 h
Lymphocyte count (per cent)	A	23.33±2.44	21.00±2.95	21.50±2.67	24.00±3.02	23.17±2.24
	B	21.83+1.54	21.33±2.04	22.33±1.69	21.83±1.58	23.17±2.24
	C	18.83±1.76	21.17±1.56	20.67±1.05	22.00±1.90	22.17±0.93
Monocyte count (per cent)	A	4.33±2.38	4.33±0.67	6.17±0.95	7.67±1.94	8.00±1.88
	B	4.33±0.80	6.33±2.12	6.67±1.41	6.67±1.36	5.83±1.14
	C	3.67±1.58	6.00±1.63	7.00±1.75	6.17±1.33	5.17±1.08
Eosinophil count (per cent)	A	4.33±1.52	6.33±1.50 *	7.00±2.42	5.50±1.45	4.67±1.02
	B	2.17+0.48	4.50+0.56	4.83+1.33	4.50+1.48	4.18±1.22
	C	5.17±1.45	3.67±2.12	4.33±1.12	3.17±1.30	4.17±0.79

* Significant at 5 per cent level as compared to the value at 0 min.

Table 7. Effect of administration of tiletamine-zolazepam on basophil count, serum glucose value and serum urea nitrogen value in dogs (Group I) (Mean ± SE)

n=6

	Sub-group	0 Min.	15 Min.	30 Min.	60 Min.	24 h
Basophil count (per cent)	A	0.17+0.17	0.17±0.17	0	0.33±0.21	0
	B	0	0.17±0.17	0	0	0
	C	0.17±0.17	0.17±0.17	0	0	0
Serum glucose (mg/dl)	A	84.72±15.53	108.14±11.68	116.07±12.70	135.89±15.60*	116.32±14.00
	B	85.12±10.37	99.41±12.11	103.57±6.05	132.14±3.06*	98.81±14.74
	C	101.73±8.99	118.35±12.41	119.19±13.35	100.51±10.46	111.01±13.08
Serum urea nitrogen (mg/dl)	A	12.54±2.86	13.46±2.47	10.16±1.52	12.27±2.18	10.50±2.05
	B	12.18±1.38	11.34+1.18	13.18+1.37	11.83±1.74	10.96±2.09
	C	9.60±1.60	11.02+2.44	10.98±1.83	10.62+1.93	11.14±2.01

* Significant at 5 per cent level as compared to the value at 0 min

Table 8. Effect of administration of tiletamine-zolazepam on serum sodium, serum potassium and serum chloride values in dogs (Group I) (Mean ± SE)

n=6

	Sub-group	0 Min.	15 Min.	30 Min.	60 Min.	24 h
Serum sodium (mEq/L)	A	104.90±6.43	103.27±9.45	110.70±14.95	105.26±13.51	100.55±8.28
	B	126.11±10.85	107.08±3.48	119.77±11.85	107.23±4.62	110.89±5.36
	C	114.68±13.36	112.51±2.44	108.27±7.29	115.41±15.91	123.50±8.92
Serum potassium (mEq/L)	A	4.98±0.17	5.17±0.17	5.11±0.27	5.36±0.32	5.45±0.35
	B	5.22±0.16	4.86±0.09	5.18±0.25	5.22±0.28	5.28±0.24
	C	5.70±0.27	5.36±0.38	5.86±0.20	5.70±0.28	5.49±0.14
Serum chloride (mEq/L)	A	104.60±7.33	117.33±6.24	113.61±9.02	121.31±5.59	102.44±6.73
	B	107.51±5.23	121.86±5.44	118.24±6.13	115.40±7.13	123.72±6.75
	C	107.83±7.91	103.37±6.60	110.85±7.60	118.41±9.55	102.99±9.32

Table 9. Effect of administration of tiletamine-zolazepam on total serum protein content serum aspartate aminotransferase (AST) value and serum alanine aminotransferase (ALT) value in dogs (Group I) (Mean ± SE)

n=6

	Sub-group	0 Min.	15 Min.	30 Min.	60 Min.	24 h
Total serum protein (g/dl)	A	5.53±0.49	4.75±0.34	5.10±0.41	5.10+0.38	5.83±0.65
	B	5.38+0.40	5.64+0.44	5.46+0.73	4.88+0.66	5.48±0.56
	C	5.56±0.34	6.00±0.48	5.48+0.21	6.18±0.45	5.65±0.56
Serum aspartate amino-transferase (units/ml)	A	39.17±6.54	43.75±10.12	51.67±11.59	54.58±13.60	54.17+15.42
	B	38.76±9.39	39.58±9.09	44.17±7.43	46.67±9.82	48.75±10.03
	C	29.17±7.26	34.58±11.24	30.00+7.44	40.50+8.21	41.25±13.67
Serum alanine amino transferase (units/ml)	A	29.33+5.55	29.67±5.20	34.67+6.10	37.00+2.95	37.00±5.05
	B	25.00+5.23	32.33+6.18	38.00±4.70	33.67+3.48	29.33±1.91
	C	29.00±4.55	29.33±3.04	30.67±4.37	27.67+5.87	34.67+6.72

GROUP II

The observations are presented in Tables 1 and 10-17

Subgroup IIA

Tiletamine-zolazepam combination at the rate of 5 mg kg bodyweight with xylazine premedication at the rate of 0 5 mg kg bodyweight was administered IM to all the animals of this subgroup

Clinical observations

Administration of xylazine brought about sedation in the animals as evidenced by winking of eyes attempts to vomit and incocrdination of movements with head down posture and tendency for sitting on the haunches

The induction time was 3 33 ± 0 62 min the effect persisted for 49 67 ± 6 43 min and the recovery time was 160 00 ± 17 70 min

The animals assumed sternal recumbency by 1 83 ± 0 40 min lateral recumbency with loss of headrighting reflex by 3 33 ± 0 62 min Loss of sensitivity to pinprick was noticed at 6 00 ± 1 16 min and the sensitivity to pinprick was found returned by 35 00 ± 2 86 min The loss of headrighting reflex persisted for 49 67 ± 6 43 min

The animals resumed sternal recumbency by 64 83 ± 7 03 min and was able to stand up with incoordination by 101 17 ± 10 52 min The gait of the animals became apparently normal by 213 00 ± 16 84 min

Salivation was scanty and the eyes were partially closed Palpebral reflexes were abolished in two animals and was sluggish in others Pupils were slightly dilated Pedal reflexes were abolished Swallowing movements were present The jaw muscles were relaxed and permitted endotracheal intubation The muscle relaxation time was 39 50 ± 5 54 min

The respiration was abdominal and regular The relaxation of the abdominal muscles and limbs was good to excellent

During recovery paddling was less prominent and vocalization was absent All the animals resumed feeding and drinking soon after recovery

In two animals laparotomy was performed to assess the depth of anaesthesia and was found to be satisfactory

Physiological observations

The rectal temperature (°C) was 39 17 ± 0 24 and 39 17 ± 0 24 before and after premedication respectively 38 9 ± 0 25 at 15 min 38 20 ± 0 20 at 30 min 37 76 ± 0 27 at 60 min and 39 06 ± 0 19 at 24 h There was gradual decrease in rectal temperature after the administration of tiletamine zolazepam and the decrease was significant (P<0 05) at 30 min and

The pulse rate (per min) was 107 00 ± 9 32 and 112 50 ± 12 45 before and after premedication respectively 118 17 ± 8 62 at 15 min 106 83 ± 6 08 at 30 min 105 17 ± 11 71 at 60 min and 108 83 ± 8 65 at 24 h There was increase in pulse rate following xylazine premedication and from 30 min onwards there was decrease and became near normal by 24 h

The respiration rate (per min) was 23 50 ± 2 16 and 17 00 ± 1 97 before and after premedication respectively 16 00 ± 2 00 at 15 min 19 33 ± 3 50 at 30 min 24 67 ± 4 11 at 60 min and 28 50 ± 4 10 at 24 h There was decrease in respiration rate during the period of anaesthesia The decrease was significant (P<0 05) at 15 min

The systolic pressure (mm Hg) was 139 67 ± 4 39 and 128 33 ± 3 07 before and after premedication respectively 130 00 ± 2 25 at 15 min 126 67 ± 3 89 at 30 min 130 67 ± 1 98 at 60 min and 132 00 ± 4 50 at 24 h There was decrease in systolic pressure following xylazine premedication and administration of tiletamine-zolazepam

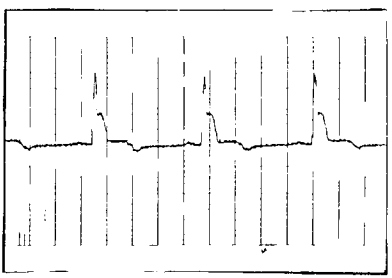
The diastolic pressure (mm Hg) was 90 00 ± 1 63 and 86 00 ± 1 03 before and after premedication respectively 82 67 ± 2 51 at 15 min 85 00 ± 2 52 at 30 min 89 33 ± 2 11 at 60 min and 85 67 ± 2 80 at 24 h There was decrease in diastolic pressure following xylazine premedication and administration of tiletamine zolazepam The decrease was significant (P<0 05) at 15 min

The coagulation time (min) of blood was 3 00 ± 0 22 and 3 67 ± 0 21 before and after premedication respectively 3 33 ± 0 33 at 15 min, 3 50 ± 0 43 at 30 min, 2 92 ± 0 20 at 60 min and 3 33 ± 0 36 at 24 h The variations were marginal

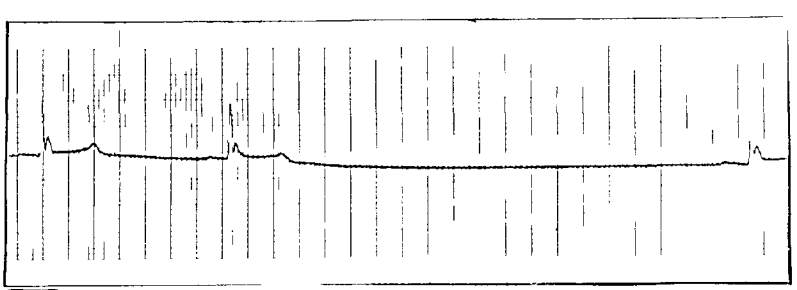
Electrocardiogram (ECG)

Increase in heart rate was noticed in two animals following the administration of xylazine and became almost normal/slightly decreased by 15 min after the administration of tiletamine-zolazepam In one animal along with increase in heart rate the amplitude of R-wave also increased following the administration of xylazine In these animals the heart rate and amplitude of R-wave became almost normal by 15 min In one animal there was no change in heart rate but the amplitude of R wave was increased after xylazine administration and became normal by 15 min but at 24 h the amplitude of R-wave was slightly increased In one animal the rhythm was irregular with increase in amplitude of R wave and occasional biphasic T-wave By 15 min the rhythm became normal but the amplitude was still higher and persisted upto 60 min In one animal there was decrease in heartrate along with occasional total blockage following xylazine administration, at 15 min and 60 min QRS complex became bifid and the T wave became depressed and at 60 min the heart rate became normal but inversion of T wave was noticed (Fig 7)

Fig 7 ECG changes following the administration of tiletamine zolazepam (5 mg/kg bodyweight) with xylazine (0 5 mg/kg bodyweight) premedication in dogs (Subgroup IIA)



A Bifid QRS complex and depression of T wave



B Decrease in heart rate with occasional total blockage

Haemogram

The erythrocyte sedimentation rate (mm/1 h) was 1 00 ± 0 00 and 1 33 ± 0 21 before and after premedication respectively, 1 50 ± 0 22 at 15 min 1 50 ± 0 22 at 30 min 1 33 ± 0 21 at 60 min and 1 33 ± 0 21 at 24 h The variations were not significant

The packed cell volume (per cent) was 36 67 ± 1 02 and 31 67 ± 0 67 before and after premedication respectively 33 00 ± 1 21 at 15 min 33 17 ± 0 83 at 30 min 33 67 ± 2 25 at 60 min and 35 33 ± 1 96 at 24 h There was reduction in PCV following the administration of xylazine as well as after the administration of tiletamine zolazepam The reduction was significant (P<0 05) after premedication and at 15 min and 30 min

The haemoglobin concentration (g/dl) was 9 37 ± 0 71 and 9 71 ± 0 77 before and after premedication respectively 10 43 ± 1 04 at 15 min 9 98 ± 0 63 at 30 min 9 21 ± 0 38 at 60 min and 10 32 ± 0 37 at 24 h The variations were marginal

The total erythrocyte count ($10^6/mm^3$) was 5 42 ± 0 12 and 4 27 ± 0 37 before and after premedication respectively 4 22 ± 0 41 at 15 min 4 13 ± 0 55 at 30 min 4 15 ± 0 20 at 60 min and 5 17 ± 0 29 at 24 h There was significant (P<0 05 decrease in total erythrocyte count after premedication and

during the period of anaesthesia and became near normal by 24 h

The total leukocyte count (10 /mm^3) was 9 12 ± 0 85 and 10 05 ± 0 74 before and after premedication respectively 10 03 ± 0 85 at 15 min 10 42 ± 1 12 at 30 min 11 28 ± 0 92 at 60 min and 10 53 ± 0 98 at 24 h The variations were marginal

The neutrophil count (per cent) was 67 17 ± 1 47 and 64 50 ± 1 61 before and after premedication respectively 66 33 ± 2 65 at 15 min 68 17 ± 2 40 at 30 min 63 17 ± 1 54 at 60 min and 63 50 ± 1 52 at 24 h There was decrease in neutrophil count following the administration of xylazine There was increase at 15 min and 30 min and thereafter there was decrease below the base line value

The lymphocyte count (per cent) was 26 67 ± 0 99 and 23 50 ± 1 59 before and after premedication respectively 22 83 ± 1 72 at 15 min 20 67 ± 1 41 at 30 min 24 00 ± 1 63 at 60 min and 24 17 ± 1 47 at 24 h There was decrease in lymphocyte count following the administration of xylazine and the decrease persisted throughout the period of anaesthesia

The monocyte count (per cent) was 3 50 ± 0 76 and 7 83 ± 1 78 before and after premedication respectively 4 33 ± 1 56 at 15 min 6 83 ± 2 24 at 30 min 6 33 ± 1 33 at 60 min and

6 50 ± 1 12 at 24 h There was significant (P<0 05) increase in the count after premedication and after induction of anaesthesia the count was decreased and thereafter there was increase

The eosinophil count (per cent) was 2 67 ± 0 67 and 3 33 ± 0 56 before and after premedication respectively 6 50 ± 1 69 at 15 min 4 17 ± 0 87 at 30 min 6 17 ± 0 87 at 60 min and 5 50 ± 1 38 at 24 h There was increase in eosinophil count following xylazine administration and the increase was more during the period of anaesthesia The increase was significant (P<0 05) at 60 min

The basophil count (per cent) was insignificant

Serum constituents

The serum glucose value (mg/dl) was 78 84 ± 9 24 and 107 96 ± 17 54 before and after premedication respectively 127 21 ± 15 12 at 15 min 146 17 ± 8 51 at 30 min 175 54 ± 9 49 at 60 min and 85 26 ± 10 43 at 24 h There was increase in serum glucose value after xylazine premedication and the increase was marked and significant (P<0 05) during the period of observation upto 60 min

The serum sodium concentration (mEq/L) was 99 82 ± 5 86 and 112 51 ± 4 85 before and after premedication respectively 109 06 ± 3 82 at 15 min 107 98 ± 4 71 at 30 min 107 43 ± 5 14

at 60 mın and 106 71 ± 5 80 at 24 h There was ıncrease ın serum sodıum concentratıon arter premedıcatıon and arter admınıstratıon of tıletamıne-zclazepam ıt was slıghtl/ reduced though above the base lıne value

The serum potassıum concentratıon (mEq/L) was 5 -4 ± 0 24 and 4 53 ± 0 22 before and after premedic-tion respectıvely 4 78 ± 0 29 at -5 mın, 5 28 ± 0 30 at 3C mın 5 29 ± 0 48 at 60 mın and 5 33 ± 0 33 at 24 h The var-a-ons were margınal

The serum chlorıde concentratıon (mEq/L) was 102 -7 ± 9 53 and 107 18 ± 5 49 before and after premedic-tion respectıvely 99 33 ± 10 89 at 15 mın 119 59 ± 9 05 at 3C mın 102 51 ± 6 15 at 60 mın and 107 62 ± 12 37 at 24 h Ther- was ıncrease ın serum chlorıde concentratıon after premedıcat-on but after tıletamıne zolazepam admınıstratıon ıt was decreased Durıng the perıod of maxımum depth of anaesthesıa ıt was -ga-n ıncreased and ıt reduced to premedıcatıon level by 60 mın

The total serum protein content (g/dı) was 5 00 ± 44 and 4 44 ± 0 61 before and after premedıcatıon respect- e-/ 4 43 ± 0 63 at 15 mın 4 94 ± 0 73 at 30 mın 4 99 ± 0 5- at 60 mın and 4 70 ± 0 65 at 24 h The varıatıons were marg-al

The serum urea nıtroger value (mg/dl) was 11 71 ± - 46 and 11 48 ± 1 19 before and after premedıcatıon respect- -

12 28 ± 1 03 at 15 min 11 97 ± 1 38 at 30 min 13 09 ± 1 46 at 60 min and 13 12 ± 1 61 at 24 h The variations were marginal

The serum aspartate aminotransferase (AST) value (units/ml) was 43 33 ± 11 13 and 50 42 ± 10 79 before and after premedication respectively 42 08 ± 9 43 at 15 min 49 17 ± 12 59 at 30 min 44 17 ± 13 41 at 60 min and 54 17 ± 10 20 at 24 h There was increase in AST value after premedication and at 15 min it was decreased During the period of maximum depth of anaesthesia (at 30 min) it was again increased At 24 h the value was slightly higher than the base line value

The serum alanine aminotransferase (ALT) value (units/ml) was 27 67 ± 2 85 and 21 33 ± 1 33 before and after premedication respectively, 23 33 ± 2 67 at 15 min 23 33 ± 4 64 at 30 min, 22 67 ± 3 78 at 60 min and 28 33 ± 1 67 at 24 h There was decrease in ALT value following xylazine premedication and during the anaesthetic period and it became near normal by 24 h

Histopathological examination

Histopathological examination revealed fatty charges in liver and presence of large number of dilated tubules and focal areas of nephrosis in kidney.

Subgroup IIB

Tiletamine zolazepam combination at the rate of 10 mg/kg bodyweight with xylazine premedication at the rate of 0 5 mg/kg bodyweight was administered IM to all the animals of this subgroup

Clinical observations

Administration of xylazine brought about sedation in the animals as evidenced by winking of eyes attempts to vomit incoordination of movements with head down posture and tendency for sitting on haunches

The induction time was 3 17 ± 0 48 min the effect persisted for 105 17 ± 10 31 min and the recovery time was 180 00 ± 14 94 min

The animals assumed sternal recumbency by 1 33 ± 0 21 min lateral recumbency with loss of headrighting reflex by 3 17 ± 0 48 min Loss of sensitivity to pinprick was noticed at 5 17 ± 0 70 min and the sensitivity to pinprick returned by 61 67 ± 5 73 min The loss of headrighting reflex persisted for 105 17 ± 10 31 min

The animals resumed sternal recumbency by 157 50 ± 28 42 min and was able to stand up with incoordination by

182 83 ± 27 99 mın The gaıt of the anımals became apparentlv normal by 288 33 ± 19 13 mın

Salıvatıon was scanty and the eyes were partıallv closed Palpebral reflexes were abolıshed ın four anımals and was sluggısh ın others Pupıls were slıghtly dılated Peda- reflexes were abolıshed Swallowıng movements were present The jaw muscles were relaxed and permıtted endotrachea- ıntubatıon The muscle relaxatıon tıme was 63 33 ± 9 06 mın

The respıratıon became abdomınal and was regular The relaxatıon of the abdomınal muscles and lımbs were excellent Durıng recovery paddlıng was absent except ın two anımals In those anımals ıt was pronounced and vocalızatıon was absent All the anımals resumed feedıng and drınkıng soon after recovery

In two anımals laparotomy was performed to assess the depth of anaesthesıa and was found to be satısfactory

Physıologıcal observatıons

The rectal temperature (°C) was 38 98 ± 0 25 and 38 93 ± 0 30 before and after premedıcatıon respectıvely 38 52 ± 0 22 at 15 mın 38 28 ± 0 18 at 30 mın 37 70 ± 0 32 at 60 mın and 38 87 ± 0 15 at 24 h There was gradual decrease ın rectal temperature after the admınıstratıon of tıletamıne zolazepam and the decrease was sıgnıfıcant ($P<0\ 05$) at 30 mın and 60 mın

The pulse rate (per mın) was 104 00 ± 5 44 and 106 67 ± 8 08 before and after premedıcatıon respectıvely 108 67 ± 6 80 at 15 mın 101 33 ± 6 21 at 30 mın, 93 67 ± 2 22 at 60 mın and 88 33 ± 4 99 at 24 h There was ıncrease ın pulse rate followıng xylazıne premedıcatıon and from 30 mın onwards there was decrease

The respıratıon rate (per mın) was 26 00 ± 2 42 and 23 00 ± 2 41 before and after premedıcatıon respectıvely 14 00 ± 3 39 at 15 mın, 12 33 ± 2 65 at 30 mın 20 33 ± 3 8º at 60 mın and 26 00 ± 1 71 at 24 h There was decrease ın respıratıon rate followıng xylazıne premedıcatıon and admınıstratıon of tıletamıne-zolazepam The decrease was sıgnıfıcant (P<0 05) at 15 mın and 30 mın and became near normal by 24 h

The systolıc pressure (mm Hg) was 144 00 ± 5 58 and 136 00 ± 4 44 before and after premedıcatıon respectıvely 130 00 ± 4 59 at 15 mın 131 67 ± 3 81 at 30 mın, 136 00 ± 5 16 at 60 mın and 142 67 ± 6 04 at 24 h There was decrease ın systolıc pressure followıng xylazıne premedıcatıon and admınıstratıon of tıletamıne zolazepam It became normal by 24 h

The dıastolıc pressure (mm Hg) was 87 33 ± 2 40 and 81 67 ± 2 33 before and after premedıcatıon respectıvely 78 33 ± 2 89 at 15 mın 82 67 ± 2 81 at 30 mın 83 00 ± 2 91

at 60 mın and 86 67 ± 2 72 at 24 h There was decrease ın dıastolıc pressure followıng xylazıne premedıcatıon and admınıstratıon of tıletamıne-zolazepam and the decrease was sıgnıfıcant (P<0 05) at 15 mın Thereafter there was gradual ıncrease and became near normal by 24 h

The coagulatıon tıme (mın) of blood was 3 50 ± 0 26 and 3 42 ± 0 20 before and after premedıcatıon respectıvely 3 50 ± 0 36 at 15 mın, 3 67 ± 0 57 at 30 mın, 3 67 ± 0 57 at 60 mın and 3 58 ± 0 24 at 24 h The varıatıons were margınal

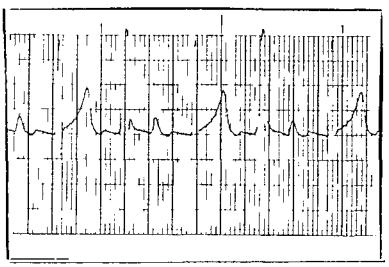
Electrocardıogram (ECG)

Slıght ıncrease ın heart rate was notıced ın four anımals followıng the admınıstratıon of xylazıne In one of these anımals there was T-wave only ın alternate beats followıng xylazıne admınıstratıon and ıncrease ın amplıtude of R wave wıth spıkıng of T-wave at 15 mın By 24 h the heart rate became normal/slıghtly hıgher and ın another anımal the T wave was bıphasıc/ınverted followıng xylazıne admınıstratıon (Fıg 8)

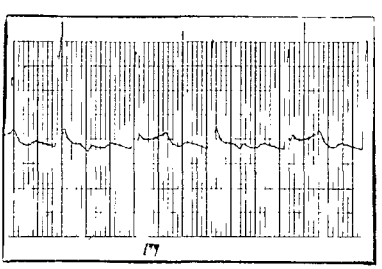
Haemogram

The erythrocyte sedımentatıon rate (mm/1 h) was 1 67 ± 0 21 and 1 33 ± 0 21 before and after premedıcatıon respectıvely 1 50 ± 0 34 at 15 mın 1 33 ± 0 21 at 30 mın

Fig 8 ECG changes following the administration of tiletamine-zolazepam (10 mg/kg bodyweight) with xylazine (0 5 mg/kg bodyweight) premedication in dogs (Subgroup IIB)



A Spiking of T-wave in alternate beats



B Biphasic/inverted T-wave

1 50 ± 0 22 at 60 mın and 1 50 ± 0 34 at 24 h The varıatıons were not sıgnıfıcant

The packed cell volume (per cent) was 37 33 ± 1 58 and 34 83 ± 1 90 before and after premedıcatıon respectıvely 34 50 ± 1 76 at 15 mın 33 17 ± 1 81 at 30 mın, 35 00 ± 2 28 at 60 mın and 34 67 ± 2 14 at 24 h There was reductıon ın PCV followıng the admınıstratıon of xylazıne as well as after the admınıstratıon of tıletamıne-zolazepam

The haemoglobın concentratıon (g/dl) was 8 81 ± 0 60 and 9 65 ± 0 90 before and after premedıcatıon respectıvely 8 91 ± 0 70 at 15 mın, 9 60 ± 1 06 at 30 mın 9 98 ± 1 36 at 60 mın and 9 43 ± 0 82 at 24 h The varıatıons were margınal

The total erythrocyte count (10^6/mm^3) was 4 75 ± 0 67 and 4 53 ± 0 68 before and after premedıcatıon respectıvely 3 85 ± 0 43 at 15 mın 4 57 ± 0 53 at 30 mın, 4 58 ± 0 33 at 60 mın and 4 97 ± 0 28 at 24 h There was decrease ın TEC after premedıcatıon and durıng the anaesthetıc perıod and became near normal by 24 h

The total leukocyte count (10^3/mm^3) was 10 70 ± 0 27 and 10 28 ± 0 67 before and after premedıcatıon respectıvely 10 87 ± 0 79 at 15 mın 10 53 ± 0 95 at 30 mın 10 10 ± 0 72 at 60 mın and 9 78 ± 0 67 at 24 h The varıatıons were margınal

The neutrophil count (per cent) was 64 17 ± 0 83 and 61 67 ± 1 45 before and after premedication respectively 64 00 ± 2 68 at 15 min 66 67 ± 2 04 at 30 min 62 17 ± 2 18 at 60 min and 66 83 ± 1 51 at 24 h There was decrease in neutrophil count following the administration of xylazine and became normal by 15 min after administration of tiletamine zolazepam

The lymphocyte count (per cent) was 23 50 ± 2 17 and 25 67 ± 1 45 before and after premedication respectively 25 17 ± 1 66 at 15 min 23 33 ± 2 04 at 30 min 23 83 ± 1 33 at 60 min and 24 17 ± 0 60 at 24 h The variations were marginal

The monocyte count (per cent) was 7 00 ± 1 63 and 5 50 ± 1 31 before and after premedication respectively 5 50 ± 1 71 at 15 min, 6 00 ± 0 89 at 30 min 7 33 ± 1 84 at 60 min and 5 17 ± 1 05 at 24 h The variations were not significant

The eosinophil count (per cent) was 5 33 ± 1 89 and 7 00 ± 2 07 before and after premedication respectively 5 33 ± 1 12 at 15 min, 3 67 ± 1 14 at 30 min, 6 33 ± 1 08 at 60 min and 3 67 ± 0 80 at 24 h There was increase in eosinophil count following the administration of xylazine Following tiletamine zolazepam administration it became normal thereafter there was increase at 60 min

The basophil count (per cent) was insignificant

Serum constituents

The serum glucose value (mg/dl) was 94 88 ± 6 12 and 124 76 ± 7 57 before and after premedication respectively 142 62 ± 14 04 at 15 min 189 05 ± 18 57 at 30 min 202 86 ± 16 49 at 60 min and 121 43 ± 5 53 at 24 h There was significant (P<0 05) increase in serum glucose value after xylazine premedication and the increase was marked and significant (P<0 05) during the period upto 24 h

The serum sodium concentration (mEq/L) was 125 55 ± 6 96 and 109 25 ± 5 62 before and after premedication respectively, 106 53 ± 4 84 at 15 min 118 30 ± 6 05 at 30 min 123 35 ± 16 09 at 60 min and 116 67 ± 11 31 at 24 h There was decrease in serum sodium concentration after premedication and during the period of anaesthesia and became normal by 60 min The decrease at 15 min was significant (P<0 05)

The serum potassium concentration (mEq/L) was 5 46 ± 0 28 and 5 10 ± 0 30 before and after premedication respectively, 5 36 ± 0 32 at 15 min 5 26 ± 0 19 at 30 min 5 42 ± 0 28 at 60 min and 5 16 ± 0 33 at 24 h The variations were marginal

The serum chloride concentration (mEq/L) was 88 40 ± 9 09 and 103 41 ± 4 75 before and after premedication respectively 91 74 ± 5 54 at 15 min 95 36 ± 4 54 at 30 min

103 41 ± 5 84 at 60 mın and 96 87 ± 6 20 at 24 h There was ıncrease ın serum chloride concentratıon followıng the admınıstratıon of xylazıne, but after tıletamıne zolazepam admınıstratıon ıt was slıghtly decreased at 15 mın and thereafter ıt was ıncreased above the base lıne value

The total serum protein content (g/dl) was 5 36 ± 0 56 and 6 23 ± 0 99 before and after premedicatıon respectıvely 5 53 ± 0 59 at 15 mın 5 50 ± 0 70 at 30 mın 5 83 ± 0 69 at 60 mın and 5 03 ± 0 55 at 24 h Though there was ıncrease ın serum protein count after premedicatıon, the varıatıons were margınal durıng the anaesthetıc perıod

The serum urea nıtrogen value (mg/dl) was 11 01 ± 1 29 and 10 33 ± 1 03 before and after premedicatıon respectıvely 9 34 ± 1 37 at 15 mın 10 74 ± 1 61 at 30 mın 11 74 ± 1 91 at 60 mın and 10 47 ± 1 98 at 24 h The varıatıons were margınal

The serum aspartate amınotransferase (AST) value (unıts/ml) was 29 17 ± 2 79 and 31 25 ± 1 91 before and after premedicatıon respectıvely 35 00 ± 7 66 at 15 mın 19 58 ± 1 50 at 30 mın 29 17 ± 3 00 at 60 mın and 36 25 ± 4 60 at 24 h There was slıght ıncrease ın AST value after premedicatıon and at 15 mın Durıng the perıod of maxımum depth of anaesthesıa (at 30 mın) ıt was decreased and at 24 h the value was hıgher than the base lıne value

The serum alanine aminotransferase (ALT) value (units/ml) was 18 67 ± 3 95 and 24 00 ± 3 54 before and after premedication respectively, 21 67 ± 4 05 at 15 min 22 33 ± 5 74 at 30 min 21 00 ± 5 31 at 60 min and 22 67 ± 3 17 at 24 h There was significant (P<0 05) increase in ALT value following xylazine premedication and though there was decrease thereafter the value remained high above the base line value

Histopathological examination

Histopathological examination revealed mild fatty change in liver and cystic dilation of tubules in kidney

Subgroup IIC

Tiletamine-zolazepam combination at the rate of 15 mg kg bodyweight with xylazine premedication at the rate of 0 5 mg kg bodyweight was administered IM to all the animals of this subgroup

Clinical observations

Administration of xylazine brought about sedation in the animals as evidenced by winking of eyes attempts to vomit and incoordination of movements with head down posture and tendency for sitting on haunches

The induction time was 2 83 ± 0 54 min the effect persisted for 125 83 ± 10 78 min and the recovery time was 181 00 ± 12 82 min

The animals assumed sternal recumbency by 1 33 ± 0 2- min lateral recumbency with loss of headrighting reflex by 2 83 ± 0 54 min Loss of sensitivity to pinprick was noticed at 5 00 ± 0 37 min and the sensitivity to pinprick was returned by 67 50 ± 9 60 min The loss of headrighting reflex persisted for 125 83 ± 10 78 min

The animals resumed sternal recumbency by 158 33 ± 10 99 min and was able to stand up with incoordination by 201 17 ± 9 19 min The gait of the animals became apparently normal by 309 67 ± 12 86 min

Salivation was scanty and the eyes were partially closed Palpebral and pedal reflexes were abolished Pupils were slightly dilated Swallowing movements were present The jaw muscles were relaxed and permitted endotracheal intubation The muscle relaxation time was 78 67 ± 9 37 min

The respiration was abdominal and regular The relaxation of the abdominal muscles and limbs was excellent

During recovery paddling and vocalization were not common All the animals resumed feeding and drinking soon after recovery

In two animals laparotomy was performed to assess the depth of anaesthesia and was found to be satisfactory

Physiological observations

The rectal temperature (°C) was 39 17 ± 0 19 and 39 20 ± 0 30 before and after premedication respectively 38 37 ± 0 28 at 15 min 38 41 ± 0 45 at 30 min 37 85 ± 0 48 at 60 min and 38 87 ± 0 14 at 24 h There was decrease in rectal temperature after the administration of tiletamine zolazepam and the decrease was significant (P<0 05) at 15 min and 60 min

The pulse rate (per min) was 103 33 ± 8 08 and 127 83 ± 6 34 before and after premedication respectively 124 33 ± 8 12 at 15 min 122 33 ± 10 20 at 30 min, 115 83 ± 12 52 at 60 min and 93 00 ± 7 08 at 24 h There was significant (P<0 05) increase in pulse xrate following xylazine premedication and there was decrease following the administration of tiletamine zolazepam, but it remained above the baseline value

The respiration rate (per min) was 26 50 ± 1 26 and 23 00 ± 2 97 before and after premedication respectively 14 3 ± 2 04 at 15 min 13 83 ± 2 07 at 30 min 18 00 ± 2 53 at 60 min and 26 50 ± 3 44 at 24 h There was decrease in respiration rate following xylazine premedication and after the administration of tiletamine zolazepam The decrease was

significant (P<0 05) at 15 min 30 min and 60 min and became normal by 24 h

The systolic pressure (mm Hg) was 147 50 ± [illegible] and 136 67 ± 3 13 before and after premedication respectively 130 33 ± 4 14 at 15 min 133 33 ± 6 19 at 30 min [illegible] at 60 min and 136 67 ± 4 61 at 24 h There was significant (P<0 05) decrease in systolic pressure following xylazine administration and at 15 min and 60 min following administration of tiletamine-zolazepam

The diastolic pressure (mm Hg) was 91 50 ± [illegible] and 85 00 ± 3 79 before and after premedication respectively 82 33 ± 1 31 at 15 min 86 00 ± 3 18 at 30 min 85 00 ± at 60 min and 87 33 ± 2 56 at 24 h There was decrease in diastolic pressure following xylazine premedication and following the administration of tiletamire zolazepam The decrease was significant (P<0 05) at 15 min

The coagulation time (min) of blood was 2 92 ± [illegible] and 3 42 ± 0 42 before and after premedication respectively 3 67 ± 0 40 at 15 min 3 42 ± 0 24 at 30 min 3 17 ± 0 28 at 60 min and 3 42 ± 0 08 at 24 h The increase in coagulation time of blood at 24 h was significant (P<0 05) but the increase was within the normal limit

Electrocardiogram (ECG)

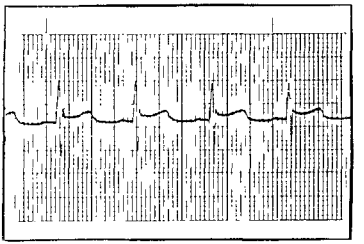
Increase in heart rate was noticed in all the animals except in one after administration of xylazine and the increase persisted upto 60 min and became normal by 24 h Depression of T wave was noticed in one animal at 15 min and became normal by 24 h In one animal depression of T wave was noticed following administration of xylazine and it persisted upto 60 min and became normal by 24 h Increase in amplitude of QRS complex was noticed in two animals at 15 min after administration of tiletamine zolazepam and became normal by 24 h (Fig 9)

Haemogram

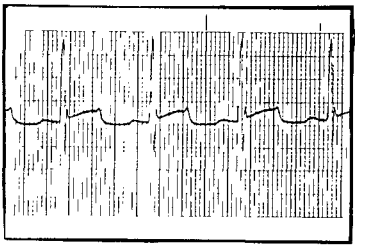
The erythrocyte sedimentation rate (mm/1 h) was 1 83 ± 0 31 and 1 67 ± 0 21 before and after premedication respectively 1 67 ± 0 33 at 15 min 1 67 ± 0 33 at 30 min 1 33 ± 0 21 at 60 min and 1 67 ± 0 33 at 24 h The variations were not significant

The packed cell volume (per cent) was 35 50 ± 0 56 and 31 50 ± 1 75 before and after premedication respectively 32 83 ± 1 74 at 15 min 33 67 ± 1 43 at 30 min 34 17 ± 0 91 at 60 min and 33 17 ± 1 40 at 24 h There was reduction in PCV following the administration of xylazine as well as following the administration of tiletamine zolazepam

9 ECG changes following the administration of tiletamine-zolazepam (15 mg/kg bodyweight) with xylazine (0 5 mg/kg bodyweight) premedication in dogs (Subgroup IIC)



A Depression of T-wave



B Increase in amplitude of QRS complex

The haemoglobin concentration (g/dl) was 11 16 ± 0 5[illegible] and 10 15 ± 0 91 before and after premedication respectively 10 71 ± 0 85 at 15 min 10 60 ± 0 96 at 30 min 10 04 ± 88 at 60 min and 11 05 ± 1 03 at 24 h The variations were marginal

The total erythrocyte count (10^6/mm) was 5 25 ± 17 and 4 93 ± 0 18 before and after premedication respectivel 4 33 ± 0 50 at 15 min 4 23 ± 0 49 at 30 min 4 57 ± 0 45 at 60 min and 4 88 ± 0 33 at 24 h There was decrease in total erythrocyte count after xylazine premedication and after the administration of tiletamine-zolazepam The decrease following xylazine premedication was significant ($P<0.05$)

The total leukocyte count (10^3/mm^3) was 10 35 ± 0 93 and 10 47 ± 0 51 before and after premedication respectively 10 98 ± 0 44 at 15 min 12 07 ± 0 48 at 30 min 12 38 ± 0 [illegible] at 60 min and 9 78 ± 0 62 at 24 h The variations were not significant

The neutrophil count (per cent) was 68 17 ± 1 4 and 66 00 ± 1 13 before and after premedication respectivel 64 8 ± 1 08 at 15 min, 64 83 ± 1 99 at 30 min, 65 67 ± 1 67 at 60 min and 63 00 ± 2 19 at 24 h There was decrease in neutrophil count following the administration of xylazine and the administration of tiletamine-zolazepam further decreased the count

The lymphocyte count (per cent) was 25 33 ± 1 [illegible] and 24 83 ± 2 01 before and after premedication respectively 21 50 ± 0 92 at 15 min 22 83 ± 1 14 at 30 min 24 [illegible] ± 1 [illegible] at 60 min and 25 17 ± 2 24 at 24 h There was decrease in lymphocyte count following the administration of xylazine and the administration of tiletamine-zolazepam further decreased the count but became normal by 24 h

The monocyte count (per cent) was 4 00 ± 0 52 and [illegible] ± 1 26 before and after premedication respectively [illegible] ± 0 [illegible] at 15 min 7 00 ± 1 75 at 30 min 4 83 ± 1 38 at 60 min and 8 17 ± 1 11 at 24 h There was increase in monocyte count following the administration of xylazine and after the administration of tiletamine-zolazepam it was further increased The increase was significant (P<0 05) at 15 min and 2-

The eosinophil count (per cent) was 2 83 ± 0 [illegible] and 4 33 ± 0 80 before and after premedication respectively [illegible] 83 ± 1 05 at 15 min, 4 83 ± 1 35 at 30 min, 4 17 ± 0 87 at 60 min and 3 67 ± 1 08 at 24 h There was increase in eosinophil count following the administration of xylazine and the increase was more during the period of anaesthesia

The basophil count (per cent) was insignificant

Serum constituents

The serum glucose value (mg/dl) was 93 33 ± 9 86 and 99 29 ± 11 32 before and after premedication respectively 126 19 ± 22 20 at 15 min 130 48 ± 25 21 at 30 min 151 00 ± 26 17 at 60 min and 87 14 ± 8 68 at 24 h There was increase in serum glucose value after xylazine premedication and the increase was more during the period of anaesthesia

The serum sodium concentration (mEq/L was 111 06 ± 3 19 and 114 94 ± 9 50 before and after premedication respectively 102 00 ± 7 29 at 15 min 112 14 ± 10 06 at 30 min, 102 54 ± 7 00 at 60 min and 124 83 ± 5 95 at 24 h There was increase in serum sodium concentration following premedication Following tiletamine zolazepam administration it was seen reduced though there was slight increase at 30 min and 24 h

The serum potassium concentration mEq/L) was 5 09 ± 0 25 and 4 85 ± 0 25 before and after premedication respectively 4 77 ± 0 27 at 15 min, 5 25 ± 0 29 at 30 min 5 01 ± 0 48 at 60 min and 4 96 ± 0 29 at 24 h The variations were marginal

The serum chloride concentration (mEq L) was 116 81 ± 5 37 and 112 48 ± 4 08 before and after premedication respectively 12- 60 ± 6 08 at 15 min 120 4- ± 5 76 at 30 min 116 91 ± 7 18 at 60 min and 112 38 ± 7 69 at 24 h There was

increase in serum chloride concentration after the administration of tiletamine-zolazepam and became normal by 60 min

The total serum protein content (g/dl) was 5 [illegible] ± 0 30 and 5 88 ± 0 26 before and after premedication respectively 6 39 ± 0 61 at 15 min 6 49 ± 0 53 at 30 min 6 33 ± 0 -4 at 60 min and 5 48 ± 0 42 at 24 h The variations were marginal

The serum urea nitrogen value (mg/dl) was 7 96 ± 0 90 and 9 39 ± 1 20 before and after premedication respectively 9 16 ± 1 39 at 15 min, 9 42 ± 1 45 at 30 min 11 03 ± 2 -5 at 60 min and 9 17 ± 1 86 at 24 h The variations were marginal

The serum aspartate aminotransferase (AST) value (units/ml) was 42 50 ± 5 77 and 47 92 ± 5 60 before and after premedication respectively 45 00 ± 8 01 at 15 min 5- 67 ± 10 26 at 30 min 57 50 ± 6 39 at 60 min and 52 92 ± [illegible] 74 at 24 h There was increase in AST value after premedication and after the administration of tiletamine-zolazepam

The serum alanine aminotransferase (ALT) value (units/ml) was 28 33 ± 3 07 and 27 67 ± 3 40 before and after premedication respectively, 27 67 ± 4 57 at 15 min 34 00 ± 5 77 at 30 min 31 67 ± 2 85 at 60 min and 32 00 ± 5 95 at 24 h After premedication the ALT value was slightly decreased and

following the administration of tiletamine-zolazepam it was increased

Histopathological examination

Histopathological examination revealed cloudy swelling and mild fatty change in liver and dilation of tubules along with foecal areas of nephrosis in kidney

Table 10. Effect of administration of tiletamine-zolazepam with xylazine premedication on rectal temperature, pulse rate and respiration rate in dogs (Group II) (Mean ± SE)

n=6

	Sub-group	0 Min.	After the admn. of xylazine	15 Min.	30 Min.	60 Min.	24 h
Rectal temperature (°C)	A	39.17±0.24	39.17±0.24	38.93±0.25	38.20±0.20 *	37.76±0.27 *	39.06±0.19
	B	38.98±0.25	38.93±0.30	38.52±0.22 *	38.28±0.18 *	37.70±0.32 *	38.87±0.15
	C	39.17±0.19	39.20±0.30	38.37±0.28	38.41±0.42	37.85±0.48	38.87±0.14
Pulse rate (per min)	A	107.00±9.32	112.50±12.45	118.17±8.62	106.83±6.08	105.17±11.71	108.83±8.65
	B	104.00±5.44	106.67±8.08	108.67±6.80	101.33±6.21	93.67±2.22	88.33±4.99
	C	103.33±8.08	127.83±6.34 *	124.33±8.12	122.33±10.20	115.83±12.52	93.00±7.98
Respiration rate (per min)	A	23.50+2.16	17.00+1.97	16.00+2.00 *	19.33+3.50	24.67+4.11	28.50+4.10
	B	26.00+2.42	23.00+2.41	14.00+3.39 *	12.33+2.65 *	20.33+3.89	26.00+1.71
	C	26.50+1.26	23.00+2.97	14.33±2.04 *	13.83±2.07 *	18.00+2.53 *	26.50+3.44

* Significant at 5 per cent level as compared to the value at 0 min.

Table 11. Effect of administration of tiletamine-zolazepam with xylazine premedication on systolic pressure, diastolic pressure and coagulation time of blood in dogs (Group II) (Mean ± SE)

n=6

	Sub-group	0 Min.	After the admn. of xylazine	15 Min.	30 Min.	60 Min.	24 h
Systolic pressure (mm Hg)	A	139.67+4.39	128.33+3.07	130.00+2.25	126.67+3.89	130.67±1.98	132.00+4.50
	B	144.00±5.58	136.00+4.44 *	130.00±4.59 *	131.67±3.81	136.00±5.16 *	142.67±6.04
	C	147.50±1.71	136.67±3.13	130.33±4.14	133.33±6.19	133.67±3.24	136.67±4.61
Diastolic pressure (mm Hg)	A	90.00±1.63	86.00±1.03	82.67±2.51 *	85.00±2.52	89.33±2.11	85.67±2.80
	B	87.33±2.40	81.67±2.33	78.33±2.89 *	82.67±2.81	83.00±2.91	86.67±2.72
	C	91.50±1.86	85.00±3.79	82.33±1.31	86.00±3.18	85.33±3.75	87.33±2.56
Coagulation time of blood (in min)	A	3.00+0.22	3.67+0.21	3.33+0.33	3.50±0.43	2.92±0.20	3.33±0.36
	B	3.50±0.26	3.42+0.20	3.50+0.36	3.67+0.57	3.67±0.57	3.58±0.24 *
	C	2.92+0.20	3.42+0.42	3.67+0.40	3.42+0.24	3.17±0.28	3.42+0.08

* Significant at 5 per cent level as compared to the value at 0 min.

Table 12. Effect of administration of tiletamine-zolazepam with xylazine premedication on erythrocyte sedimentation rate, packed cell volume and haemoglobin concentration in dogs (Group II) (Mean ± SE)

n=6

	Sub-group	0 Min.	After the admn. of xylazine	15 Min.	30 Min.	60 Min.	24 h
Erythrocyte sedimentation rate (mm/1 h)	A	1.00+0.00	1.33+0.21	1.50+0.22	1.50±0.22	1.33±0.21	1.33±0.21
	B	1.67±0.21	1.33±0.21	1.50±0.34	1.33±0.21	1.50±0.22	1.50±0.34
	C	1.83±0.31	1.67±0.21	1.67±0.33	1.67±0.33	1.33±0.21	1.67±0.33
Packed cell volume (per cent)	A	36.67±1.02	31.67±0.67 *	33.00±1.21 *	33.17+0.83 *	33.67±2.25	35.33+1.96
	B	37.33+1.58	34.83±1.90	34.50±1.76	33.17±1.81	35.00±2.28	34.67±2.14
	C	35.50±0.56	31.50±1.75	32.83±1.74	33.67±1.43	34.17±0.91	33.17±1.40
Haemoglobin concentration (g/dl)	A	9.37+0.71	9.71+0.77	10.43±1.04	9.98+0.63	9.21±0.38	10.32±0.37
	B	8 81+0.60	9 65+0.90	8 91+0.70	9.60+1.06	9.98+1.36	9.43+0.82
	C	11.16+0.55	10.15±0.91	10.71±0.85	10.60+0.96	10.04+0.88	11.05+1.03

* Significant at 5 per cent level as compared to the value at 0 min.

Table 13. Effect of administration of tiletamine-zolazepam with xylazine premedication on total erythrocyte count, total leukocyte count and neutrophil count in dogs (Group II) (Mean ± SE)

n=6

	Sub-group	0 Min.	After the admn. of xylazine	15 Min.	30 Min.	60 Min.	24 h
Total erythrocyte count (10^6/mm^3)	A	5.42±0.12	4.27±0.37 *	4.22±0.41 *	4.13±0.55 *	4.15±0.20 *	5.17±0.29
	B	4.75±0.67	4.53±0.68	3.85±0.43	4.57±0.53	4.58±0.33	4.97±0.28
	C	5.25±0.17	4.93±0.18 *	4.33±0.50	4.23±0.49	4.57±0.45	4.88±0.33
Total leukocyte count (10^3/mm^3)	A	9.12±0.85	10.05±0.74	10.03±0.85	10.42±1.12	11.28±0.92	10.53±0.98
	B	10.70±0.27	10.28±0.67	10.87±0.79	10.53±0.95	10.10±0.72	9.78±0.67
	C	10.35±0.93	10.47±0.51	10.98±0.44	12.07±0.48	12.38±0.50	9.78±0.62
Neutrophil count (per cent)	A	67.17±1.47	64.50±1.61	66.33±2.65	68.17±2.40	63.17±1.54	6.35 ±1.52
	B	64.17±0.83	61.67±1.45	64.00±2.68	66.67±2.04	62.17±2.18	66.83±1.51
	C	68.17±1.14	66.00±1.13	64.83±1.08	64.83±1.99	65.67±1.67	63.00±2.19

* Significant at 5 per cent level as compared to the value at 0 min.

Table 14. Effect of administration of tiletamine-zolazepam with xylazine premedication on lymphocyte, monocyte and eosinophil counts in dogs (Group II) (Mean ± SE)

n=6

	Sub-group	0 Min.	After the admn. of xylazine	15 Min.	30 Min.	60 Min.	24 h
Lymphocyte count (per cent)	A	26.67±0.99	23.50±1.59	22.83±1.72	20.67±1.41	24.00±1.63	24.17±1.47
	B	23.50+2.17	25.67+1.45	25.17+1.66	23.33+2.04	23.83±1.33	24.17+0.60
	C	25.33±1.73	24.83+2.01	21.50±0.92	22.83±1.14	24.83±1.11	25.17±2.24
Monocyte count (per cent)	A	3.50+0.76	7.83±1.78 *	4.33±1.56	6.83+2.24	6.33±1.33	6.50±1.12
	B	7.00±1.63	5.50±1.31	5.50±1.71	6.00±0.89	7.33±1.84	5.17±1.05
	C	4.00±0.52	4.67±1.26	7.00±0.73 *	7.00±1.75	4.83±1.38	8.17±1.11 *
Eosinophil count (per cent)	A	2.67±0.67	3.33±0.56	6.50±1.69	4.17+0.87	6.17±0.87 *	5.50±1.38
	B	5.33+1.89	7.00±2.07	5.33±1.12	3.67±1.14	6.33±1.08	3.67±0.80
	C	2.83±0.87	4.33±0.80	4.83±1.05	4.83+1.35	4.17+0.87	3.67±1.08

* Significant at 5 per cent level as compared to the value at 0 min.

Table 15. Effect of administration of tiletamine-zolazepam with xylazine premedication on basophil count, serum glucose value and serum urea nitrogen value in dogs (Group II) (Mean ± SE)

n=6

	Sub-group	0 Min.	After the admn. of xylazine	15 Min.	30 Min.	60 Min.	24 h
Basophil count (per cent)	A	0	0	0	0.17+0.17	0.33±0.21	0
	B	0	0	0	0	0.17±0.17	0
	C	0	0	0	0.17±0.17	0.17±0.17	0
Serum glucose (mg/dl)	A	78.84±9.24	107.96±17.54	127.21±15.12*	146.17±8.51*	175.54±9.49*	85.26±10.43
	B	94.88±6.12	124.76±7.57*	142.62±14.04*	189.05±18.57*	202.86±16.49*	121.43±5.53*
	C	93.33±9.86	99.29±11.32	126.19±22.20	130.48±25.21	151.00±26.17	87.14±8.68
Serum urea nitrogen (mg/dl)	A	11.71+1.46	11.48+1.19	12.28+1.03	11.97+1.38	13.09+1.46	13.12±1.61
	B	11.01±1.29	10.33±1.03	9.34±1.37	10.74±1.61	11.74±1.91	10.47±1.98
	C	7 96+0.90	9.39+1.20	9.16+1.39	9.42±1.45	11.03+2.45	9.17+1.86

* Significant at 5 per cent level as compared to the value at 0 min.

Table 16. Effect of administration of tiletamine-zolazepam with xylazine premedication on serum sodium, serum potassium and serum chloride values in dogs (Group II) (Mean ± SE)

n=6

	Sub-group	0 Min.	After the admn. of xylazine	15 Min.	30 Min.	60 Min.	24 h
Serum sodium (mEq/L)	A	99.82+5.86	112.51±4.85	109.06±3.82	107.98±4.71	107.43±3.14	106.71±5.80
	B	125.55±6.96	109.25±5.62	106.53±4.84*	118.30±6.05	123.35±16.09	116.67±11.31
	C	111.06±3.19	114.94±9.50	102.00±7.29	112.14±10.06	102.54±7.00	124.83±5.95
Serum potassium (mEq/L)	A	5.24±0.24	4.53±0.22	4.78±0.29	5.28±0.30	5.29±0.48	5.33±0.33
	B	5.46±0.28	5.10±0.30	5.36±0.32	5.26±0.19	5.42±0.28	5.16±0.33
	C	5.09±0.25	4.85±0.25	4.77±0.27	5.25±0.29	5.01±0.48	4.96±0.29
Serum chloride (mEq/L)	A	102.67±9.53	107.18+5.49	99.33±10.89	119.59±9.05	102.51±6.15	107.62±12.37
	B	88.40±9.09	103.41±4.75	91.74±5.54	95.36+4.54	103.41±5.84	96.87±6.20
	C	116.81+5.37	112.48+4.08	124.60+6.08	120.44+5.76	116.91+7.18	112.38+7.69

* Significant at 5 per cent level as compared to the value at 0 min.

Table 17. Effect of administration of tiletamine-zolazepam with xylazine premedication on total serum protein content, serum aspartate aminotransferase (AST)value and serum alanine aminotransferase (ALT) value in dogs (Group II) (Mean ± SE)

n=6

	Sub-group	0 Min.	After the admn. of xylazine	15 Min.	30 Min.	60 Min.	24 h
Total serum protein (g/dl)	A	5.00±0.44	4.44±0.61	4.43±0.63	4.94±0.73	4.99±0.57	4.70±0.65
	B	5.36±0.56	6.23±0.99	5.53±0.59	5.50±0.70	5.83±0.69	5.03±0.55
	C	5.34±0.30	5.88±0.26	6.39±0.61	6.49±0.53	6.33±0.44	5.48±0.42
Serum aspartate amino-transferase (units/ml)	A	43.33±11.13	50.42±10.79	42.08±9.43	49.17±12.59	44.17±13.41	54.17±10.20
	B	29.17±2.79	31.25±1.91	35.00±7.66	19.58±1.50	29.17±3.00	36.25±4.60
	C	42.50±5.77	47.92±5.60	45.00±8.01	51.67±10.26	57.50±6.39	52.92±8.74
Serum alanine amino-transferase (units/ml)	A	27.67±2.85	21.33+1.33 *	23.33±2.67	23.33±4.64	22.67±3.78	28.33±1.67
	B	18.67±3.95	24.00±3.54	21.67±4.05	22.33±5.74	21.00±5.31	22.67±3.17
	C	28.33+3.07	27.67±3.40	27.67±4.57	34.00±5.77	31.67+2.85	32.00±5.95

* Significant at 5 per cent level as compared to the value at 0 min.

Discussion

DISCUSSION

The experimental study was conducted on 36 adult non descript dogs of either sex Atropine sulphate at the rate of 0 04 mg/kg bodyweight was administered IM 15 minutes prior to the administration of the experimental drugs in all the dogs The animals were randomly divided into two groups viz Group I and Group II each consisting of 18 animals Group I and II were further divided into three subgroups, viz A B and C consisting of six animals each

Tiletamine-zolazepam (T-Z) combination was administered IM at the rate of 5 mg 10 mg and 15 mg/kg bodyweight in the subgroups IA IB and IC respectively Xylazine at the rate of 0 5 mg/kg bodyweight and 15 min later, T-Z combination at the rate of 5 mg, 10 mg and 15 mg/kg bodyweight were administered IM in the subgroups IIA IIB and IIC respectively

Evaluation of anaesthesia for surgery includes continuous monitoring of clinical signs, physiological and haematological parameters In veterinary surgery the transformation of the conscious animal to the quiet state of anaesthesia and duration of anaesthesia and uneventful recovery are very important for the clinician Considering this the observations are discussed hereunder

Clinical observations

Smooth induction of anaesthesia in the shortest time poss ble has been the advantage of intravenous anaesthesia With the use of intramuscular agents in the present study the induction time was 6 17 ± 1 01 min 4 33 ± 0 21 min and 4 33 ± 0 49 min in subgroups IA IB and IC respectively, whereas it was 3 33 ± 0 62 min 3·17 ± 0 48 min and 2 83 ± 0 54 min in subgroups IIA IIB and IIC respectively It was seen that the increase in the dose of T Z reduced the induction time and premedication with xylazine reduced the induction time still further The induction with xylazine premedication was rapid and smooth This is in agreement with the observation in horses (Abrahasen *et al* 1991) It was also seen that at the dose rate of 10 mg/kg and 15 mg/kg the induction time was almost the same Stander and Morkel (1991) employed T Z for field immobilization of lions and reported that the onset of immobilization was similar for both low and high dosages

Testing of analgesia by pinprick method revealed that the sensitivity to pinprick was sluggish, indicating poor analgesia following the administration of tiletamine zolazepam but premedication with xylazine brought about satisfactory analgesia The duration of insensitivity to pinprick persisted for 29 00 ± 3 37 min 59 83 ± 6 40 min and 65 83 ± 9 86 min in subgroup IIA IIB and IIC respectively But in cats

administration of T Z alone had been reported to produce excellent analgesia (Ko *et al* 1993)

Excess salivation was the most common side effect encountered in wild and exotic carnivores following the administration of tiletamine zolazepam (Boever *et al* 1977) In the present study salivation was scanty in both the groups probably due to the prior administration of atropine Nowrozian *et al* (1981) reported suppression of salivation when atropine and xylazine was combined with ketamine Presence of salivation in tiletamine zolazepam anaesthesia may not create problem since swallowing reflexes are present (Bush *et al* 1990)

The onset of effect of tiletamine zolazepam was characterised by the winking of eyes followed by yawning licking and protrusion of tongue The eyes remained open and pupils were slightly dilated The same type of clinical symptoms were reported in cats following the administration of tiletamine (Bennett, 1969) In the present study the palpebral and pedal reflexes and swallowing movements were not abolished Silverman *et al* (1983) also reported retention of pedal and swallowing reflexes in rats mice and hamsters under tiletamine zolazepam anaesthesia Retention of laryngeal and pharyngeal reflexes had been reported in non human primates following the administration of tiletamine zolazepam Euds

1976) Retention of swallowing reflex protect the animals from aspiration of vomitus (Krahwinkel, 1970) A rhythmic side to side head movements were noticed during the induction period in most of the animals (Bree *et al* 1972)

Administration of xylazine brought about sedation in animals as evidenced by winking of eyes attempts to vomit incoordination of movements with head down posture and tendency for sitting on haunches The rhythmic side to side head movements that were manifested by the animals following the administration of tiletamine-zolazepam was not observed in animals with xylazine premedication

The animals which were administered tiletamine zolazepam with xylazine premedication the eyes were partially closed and palpebral and pedal reflexes were abolished but the swallowing movements were not abolished Protrusion of tongue though present, was not to the extent that was observed after administration of tiletamine-zolazepam alone Protrusion of tongue following the administration of xylazine had been reported in steers by Raptopoulos and Weaver (1984)

The duration of effect persisted for 33 67 ± 5 88 min 57 83 ± 6 17 min and 89 00 ± 2 86 min in subgroups IA IB and IC respectively whereas it persisted for 49 67 ± 6 6-3 min 105 ± 10 31 min and 125 83 ± 10 78 min in subgroups II- IIB and IIC respectively An increase in the dose of tiletamine zolazepam

had prolonged the duration of anaesthesia This is in agreement with the observation in chinchillas (Schulz and Fowler 1974) Premedication with xylazine had still further prolonged the duration of anaesthesia Hence it could be inferred that xylazine had an additive effect when combined with tiletamine zolazepam in prolonging the duration of anaesthesia Prolongation of the duration of anaesthesia with xylazine premedication in cats had been reported by Waterman 1983) King *et al* (1977 used tiletamine-zolazepam for the immobilization of lions and leopards and reported a highly significant positive linear relationship between the duration of anaesthesia and the dosage of the drugs

The jaw musculature maintained the tonus with the lower doses of tiletamine-zolazepam But with the highest dose in this study (15 mg/kg bodyweight), the jaw muscles though not fully relaxed permitted endotracheal intubation Marked tonus in jaw musculature had been reported in dogs following the administration of tiletamine-zolazepam (Hatch *et al* 1988) Administration of tiletamine-zolazepam with xylazine premedication resulted in the relaxation of the jaw muscles and permitted endotracheal intubation and the muscle relaxation time varied from 39 50 ± 5 54 to 78 67 ± 9 37 minutes depending upon the doses of the anaesthetics studied

Relaxation of the abdominal muscles were moderate to good when tiletamine zolazepam alone was administered whereas it was excellent with xylazine premedication Incomplete relaxation of the muscles in dogs (Fieni and Tainturier 1993) and cats (Chen and Ensor 1968) had been reported following the administration of tiletamine-zolazepam Short (1987) reported that the muscle relaxation produced by the dissociative agents such as ketamine and tiletamine was very poor when used alone and became more satisfactory when combined with benzodiazepine Hence it could be inferred that the moderate to good muscle relaxation produced due to the administration of tiletamine zolazepam is due to the effect of the benzadiazepine zolazepam and the excellent degree of muscle relaxation obtained following the administration of tiletamine-zolazepam-xylazine is due to the additive effect of xylazine Improvement in the degree of muscle relaxation had been reported in horses when xylazine was combined with tiletamine-zolazepam (Hubbell *et al* 1989)

The recovery time was 111 50 ± 14 53 min 116 50 ± 10 46 min and 180 33 ± 10 57 min in subgroups IA IB and IC respectively whereas it was 160 00 ± 17 70 min 180 00 ± 14 94 min and 181 06 ± 12 82 min in subgroups IIA IIB and IIC respectively Increase in the dose of tiletamine zolazepam had prolonged recovery time and xylazine premedication still further prolonged the time During recovery paddling and vocalization were common in dogs administered with tiletamine-zolazepam but

in dogs premedicated with xylazine paddling and vocalization were not seen in all animals and recovery was smooth The increased muscular activity shown by the animals during the recovery phase following the administration of tiletamine zolazepam may be due to the lesser plasma halflife of zolazepam compared to tiletamine (Schobert, 1987 and Donaldson *et al* 1989 From the present study it could be noted that administration of xylazine due to its tranquilization effect, is helpful in making the recovery smooth

Analgesia as tested by pinprick method revealed that at the dosages studied the administration of tiletamine zolazepam alone was insufficient for carrying out surgical procedures whereas when premedicated with xylazine there was satisfactory analgesia The surgical procedure carried out on the animals confirmed that with xylazine premedication the depth of anaesthesia and muscle relaxation produced were satisfactory

Physiological observations

Administration of tiletamine-zolazepam at the rate of 5 mg/kg bodyweight did not alter the rectal temperature but at the rates of 10 mg and 15 mg/kg bodyweight reduced the rectal temperature Administration of xylazine alone at the rate of 0 5 mg/kg bodyweight did not alter the rectal temperature But administration of tiletamine zolazepam with xylazine premedication decreased the rectal temperature Dissoc ati e

anaesthetics like ketamine, by virtue of their action on the limbic-hypothalamus centres or due to increased skeletal muscle movements, was reported to increase the body temperature in dogs (Muir *et al* 1977) A decrease in rectal temperature had been reported following the administration of xylazine in buffalo calves (Peshin and Kumar 1983) and diazepam in goats (Kumar and Thurmon, 1977)

Marked increase in pulse rate was observed following the administration of tiletamine-zolazepam, but with xylazine premedication the increase was not to that extent Increase in heart rate following the administration of tiletamine zolazepam had been reported in sheep (Lagutchik *et al* 1991) whereas decrease in heart rate had been reported in dogs following the administration of xylazine (Haskins *et al*, 1975 Klide *et al* 1975 and Peshin *et al* 1980)

Respiration rate decreased following the administration of tiletamine zolazepam with and without xylazine premedication Decrease in respiration rate had been reported in dogs following the administration of xylazine (Peshin *et al* 1980 and Lele and Bhokre, 1985) and in cats following the administration of tiletamine (Calderwood *et al* 1971)

The rectal temperature, pulse rate and respiration rate were found to be near normal by 24 hours and the animals resumed

normal feeding habits indicating that the changes were transient without any untoward effect

The systolic pressure was not seen altered much with tiletamine-zolazepam administration but there was decrease with xylazine premedication Decrease in systolic pressure had been reported in dogs following the IV administration of tiletamine zolazepam (Hellebrekers *et al* 1989)

A mild increase in diastolic pressure was observed following the administration of tiletamine zolazepam and with xylazine premedication it was decreased and the decrease was significant ($P<0.05$) at 15 min A mild initial increase in mean arterial pressure had been reported in sheep following the administration of tiletamine-zolazepam (Lagutchik *et al* 1991 An increase in blood pressure, after an initial decrease had been reported during tiletamine-zolazepam anaesthesia in calves (Lin *et al* 1989) and the effect was reverse when combined with xylazine (Lin *et al* 1991) Decrease in blood pressure had been reported in cats (Colby and Sanford, 1981) and rabbits (Popilskis *et al* 1991) following administration of xylazine ketamine combination and in sheep (Lin *et al* 1993) with xylazine tiletamine zolazepam combination

The changes in the coagulation time of blood following the administration of tiletamine-zolazepam alone and with xylazine premedication were within the normal limits

Electrocardiogram (ECG)

Increase in heart rate with depression of T wave was noticed in the animals of both the groups Biphasic T wave and spiking of T wave were the common findings when tiletamine zolazepam alone was administered Whereas when premedicated with xylazine there was increase in the amplitude of QRS complex Since all the changes were found corrected spontaneously it may be inferred that the effect of the drugs on heart rate and myocardium are transient Increase in heart rate following the administration of tiletamine zolazepam had been reported in sheep (Lagutchik *et al* 1991

The mild and transient variations in blood pressure in the present study when reviewed with the pulse rate and ECG findings are suggestive of a stable cardiovascular function under the influence of the anaesthetics

Haemogram

There was slight decrease in the erythrocyte sedimentation rate following the administration of tiletamine zolazepam but in those premedicated with xylazine there was no

change Increase in ESR had been reported in buffaloes following the administration of xylazine (Sharif *et al* 1991 From this it could be inferred that xylazine premedication is helpful in maintaining the ESR in normal limits when tiletamine zolazepam is employed for inducing anaesthesia in dogs

Reduction in the packed cell volume was observed following the administration of tiletamine zolazepam with and without xylazine premedication The reduction was more with xylazine premedication Reduction in PCV had been reported in dogs following the administration of xylazine (Peshin *et al* 1980)

Slight decrease in haemoglobin concentration was noticed when tiletamine-zolazepam was administered at the rate of 15 mg/kg bodyweight But with xylazine premedication there was no change, trough Peshin *et al* (1980) had reported a decrease in haemoglobin concentration in dogs following the administration of xylazine

Decrease in total erythrocyte count was noticed following the administration of tiletamine zolazepam and the decrease was more when premedicated with xylazine A decrease in TEC was reported by Peshin *et al* (1980) in dogs following the administration of xylazine

The total leukocyte count was seen increased with the administration of tiletamine-zolazepam at the dose rates of 5 mg and 10 mg/kg bodyweight but at the dose rate of 15 mg/kg it was seen decreased Administration of tiletamine zolazepam with xylazine premedication did not alter the count Pande *et al* (1991) observed a significant increase in the count in dogs following the administration of diazepam-ketamine-atropine combination and opined that the higher values of the leukocytes obtained in the study might be related to the adrenal corticoids released to combat stress

Decrease in lymphocyte count with increase in neutrophil count had been observed following the administration of tiletamine-zolazepam at the rate of 5 mg/kg bodyweight with and without xylazine premedication Decrease in lymphocyte count with increase in neutrophil count had been reported in dogs following the administration of xylazine (Peshin *et al* 1980)

At the dose rates of 10 mg and 15 mg/kg bodyweight there was increase in lymphocyte count with decrease in neutrophil count but xylazine premedication brought about a decrease or no alteration in the count of lymphocytes Monocyte and eosinophil counts revealed and increasing tendency and the basophil count remained insignificant

Serum constituents

There was marked increase in the serum glucose value following the administration of tiletamine-zolazepam and with xylazine premedication the increase was almost double Increase in glucose value had been reported in dogs following the administration of atropine-xylazine-ketamine combination in dogs (Stephenson *et al* 1978) and after administration of ketamine xylazine in springbok (Jacobson, 1983) The reason for hyperglycemia during anaesthesia has been attributed to decreased membrane transport of glucose decreased renal excretion and decreased glucose utilization (Greene 1972

Serum sodium concentration was found decreased following the administration of tiletamine-zolazepam but with xylazine premedication there was an initial increase followed by a decrease Serum potassium concentration showed marginal variations following the administration of tiletamine zolazepam with and without xylazine premedication Serum chloride concentration was found increased with the administration of tiletamine-zolazepam at the dose rates of 5 mg and 10 mg kg bodyweight but with xylazine premedication an initial increase was followed by a decrease in values Tiletamine-zolazepam at the dose rate of 15 mg/kg bodyweight produced a biphasic decrease in serum chloride concentration and with xylazine premedication an initial decrease was followed by an increase But all the changes in serum electrolytes were within normal

physiological limits No significant change in serum electrolytes (Na+ K+ and Cl-) was observed after administration of xylazine in buffalo calves (Peshin and Kumar 1983) and plasma electrolytes concentration after administration of diazepam-ketamine in calves (Singh *et al* 1991)

The total serum protein content remained unaffected in both the groups This is in agreement with the observation in dogs following the administration of atropine-xylazine ketamine combination (Stephenson *et al* 1978) in calves following the admiristration of xylazine (Peshin and Kumar, 1983) and in goats following the administration of diazepam with and witnout atropine premedication (Kumar and Thurmon, 1977)

Considering the changes observed in the haemogram serum electrolytes (Na+ K+ and Cl-) and total serum protein content it could be inferred that the regimen of anaesthetics did not cause marked haemodilution or haemoconcentration The mild and transient variations noticed were probably due to stress pooling of blood in the spleen or slight shift of fluid from the extravascular to the intravascular compartments (Peshin and Kumar 1983 and Malek *et al* 1988)

The serum urea nitrogen value was not seen altered following the administration of tiletamine-zolazepam with and without xylazine premedication Lowering of blood urea nitrogen

value in rabbits had been reported by Popilskis *et al* (1991) following the administration of tiletamine-zolazepam xylazine and ketamine-xylazine combinations Stephenson *et al* (1978) reported that the changes in serum urea nitrogen values were within the normal range following the administration of atropine-xylazine combination in dogs No significant change in blood urea nitrogen value was reported following the administration of ketamine-xylazine combination in springbok (Jacobson, 1983)

The serum aspertate aminotransferase (AST) value was slightly increased following the administration of tiletamine zolazepam with and without xylazine premedication Stephenson *et al* (1978 reported that the changes in serum AST level following the administration of atropine-xylazine ketamine combination in dogs were within the normal range

The serum alanine aminotransferase (ALT) value was slightly increased following the administration of tiletamine zolazepam With xylazine premedication there was an initial decrease followed by a gradual increase during the anaesthetic period Slight decrease in ALT value nad been reported in buffalo calves following the administration of xylazine with and without atropire premedication (Peshin and Kumar 1983)

High ALT activity in canine liver and AST activity in almost all the tissues in various species of animals were reported on tissue analysis (Cornelius *et al* 1959) The measurement of ALT activity was reported to be liver specific in the dog (Vleet and Alberts 1968) The slight increase in ALT value in the present study is suggestive of possible liver damage consequent on the administration of the anaesthetic

Histopathological examination

In this study the histopathological examination of liver revealed cloudy swelling and mild fatty changes Kidney specimens revealed cystic dilation of the renal tubules and focal areas of nephrosis Histopathological studies of kidney in syrian hamsters following the administration of tiletamine zolazepam-xylazine combination revealed no lesion of nephrotoxicity Forsythe *et al* 1992), whereas in rabbits tiletamine-zolazepam produced nephrotoxicity (Brammer *et al* 1991)

Histopathological findings in the liver and kidney when considered with the non significant changes in serum aspertate aminotransferase alanine aminotransferase total protein and urea nitrogen levels suggest that the anaesthetics produced very little systemic injury

Summary

SUMMARY

The experimental study was conducted on 36 adult non-descript dogs of either sex The animals were randomly divided into two groups (Group I and II) consisting of 18 animals each Each group was further divided into three subgroups, viz A B and C, consisting of six animals each

Atropine sulphate (0 04 mg/kg bodyweight was administered IM 15 minutes prior to the administration of the experimental drugs in all the dogs Tiletamine zolazepam (T Z combination was administered IM at the rate of 5 mg 10 mg and 15 mg/kg bodyweight in the subgroups IA, IB and IC respectively Xylazine at the rate of 0 5 mg/kg bodyweight and 15 min later T-Z combination at the rate of 5 mg, 10 mg and 15 mg/kg bodyweight were administered IM in the subgroups IIA IIB and IIC respectively

The induction time was 6 17 ± 1 01 min 4 33 ± 0 21 min and 4 33 ± 0 49 min in subgroups IA, IB and IC respectively and 3 33 ± 0 62 min 3.7 ± 0 48 min and 2 83 ± 0 54 min in subgroups IIA IIB and IIC respectively Increase in the dose of T Z reduced the induction time and premedication with Xylazine further reduced the induction time and induction was smooth

The onset of effect of tiletamine-zolazepam was characterised by the winking of eyes yawning licking and protrusion of tongue The eyes remained open and pupils were slightly dilated The palpebral and pedal reflexes and swallowing movements were not abolished Salivation was scanty in both the groups

In the animals of Group II the eyes were partially closed and palpebral and pedal reflexes were abolished but the swallowing movements were not Protrusion of tongue though present was not to the extent that was observed in the animals of Group I Rhythmic side to side head movements were noticed during induction in all the animals of Group I but not in animals of Group II

The duration of anaesthesia was 33 67 ± 5 88 min 57 83 ± 6 17 min and 89 00 ± 2 86 min in subgroups IA, IB and IC respectively, whereas it was for 49 67 ± 6 643 min 105 17 ± 10 31 min and 125 83 ± 10 78 min in subgroups IIA, IIB and IIC respectively An increase in the dose of tiletamine zolazepam had prolonged the duration of anaesthesia and premedication with xylazine produced still longer duration of anaesthesia

The jaw musculature maintained the tonus with the lower doses of tiletamine zolazepam but at 15 mg/kg bodyweight the jaw muscles though not fully relaxed permitted endotracheal intubation Administration of tiletamine

zolazepam with xylazine resulted in relaxation of the jaw muscles and permitted endotracheal intubation Relaxation of the abdominal muscles were moderate to good when tiletamine zolazepam alone was administered, whereas it was excellent with xylazine premedication

Administration of tiletamine-zolazepam alone was found insufficient for carrying out surgical procedures but with xylazine premedication muscle relaxation and analgesia was satisfactory

The recovery time was 111 50 ± 14 53 min 116 50 ± 10 46 min and 180 33 ± 10 57 min in subgroups IA IB and IC respectively, and it was 160 00 ± 17 70 min 180 00 ± 14 94 min and 181 06 ± 12 82 min in subgroups IIA IIB and IIC respectively Increase in the dose of tiletamine zolazepam had delayed recovery and xylazine premedication delayed it still further During recovery paddling and vocalization were common in dogs of Group I but not in dogs of Group II

Reduction in rectal temperature was observed only in animals of subgroups IB and IC and in all the animals of Group II Marked increase in pulse rate was observed in Group I than in Group II Respiration rate was decreased in both the groups

A mild increase in diastolic pressure was observed in Group I The systolic and diastolic pressures were seen decreased in Group II The changes in the coagulation time of blood was within the normal limits in both the groups

Increase in heart rate with depression of T wave biphasic T wave and spiking of T-wave were the changes in electrocardiogram But the changes were corrected spontaneously

There was slight decrease in the erythrocyte sedimentation rate in animals of Group I but there was no change in Group II

Reduction in the packed cell volume was observed in both the groups but it was more, after xylazine premedication

Slight decrease in haemoglobin concentration was noticed in subgroup IC But there was no change in Group II

Decrease in total erythrocyte count was noticed in both the groups and the decrease was more when premedicated with xylazine

The total leukocyte count was seen increased in subgroup IA and IB but it was seen decreased in subgroup IC but there was no change in Group II

Decrease in lymphocyte count with increase in neutrophil count was observed in subgroups IA and IIA In subgroups IB and IC there were increase in lymphocyte count with decrease in neutrophil count but in subgroups IIB and IIC a decrease or no alteration in the count of lymphocytes was observed Monocyte and eosinophil counts were increased and the basophil count remained insignificant

There was marked increase in the serum glucose value following the the administration of tiletamine-zolazepam and with xylazine premedication the increase was more

No significant change was observed in the serum electrolytes (Na K and Cl), total serum protein content and serum urea nitrogen value in both the groups

Slight increase in serum aspartate aminotransferase (AST) and serum alanine aminotransferase (ALT) values were observed in Group I and in Group II there was increase in AST value but the ALT value decreased initially and was followed by an increase

Histopathological examination of liver revealed cloudy swelling and mild fatty changes and kidney revealed cystic dilation of the renal tubules along with focal areas of nephrosis

The following conclusions could be drawn from the study

1 Tiletamine zolazepam alone administered IM was not sufficient to produce surgical anaesthesia in dogs in the doses studied

2 Premedication with xylazine followed by administration of tiletamine zolazepam produced quick and smooth induction sufficient duration of anaesthesia and smooth recovery

3 The changes in cardiovascular and respiratory systems and blood and serum constituents were transient and were corrected spontaneously

4 Mild changes in liver and kidney observed with the doses of drugs studied suggest that the drugs have to be used with caution

5 Premedication with atropine (0 04 mg/kg bodyweight) and xylazine (0 5 mg/kg bodyweight) followed by administration of tiletamine-zolazepam (10 mg/kg bodyweight) can be adopted safely in dogs for surgery

References

REFERENCES

Abrahamsen, E J J A E Hubbell, R M Bednarski W W Muir and B A Macioce (1991) Xylazine and tiletamine zolazepam for induction of anaesthesia maintained with halothane in 19 horses *Equine Vet J* **23** (3) 224 225

Benjamin M M (1978) *Outline of Veterinary Clinical Pathology* The Iowa State University Press, Ames, USA 3rd ed pp 168 16-

Bennett, R R (1969) The clinical use of 2 (Ethylamino -2-(2-Thienyl) cyclohexanone HCl (CI 634 as an anaesthetic for the cat *Am J Vet Res* 30 (8 1469-1470

Boever, W I J Holden and K K Kane (1977) Use of Telazol (CI-744) for chemical restraint and anaesthesia in wild and exotic carnivores *Vet Med /Small Anim Clin* 72 (11) 1722 1726

Brammer, D W , B J Doerning, C E Chrisp and H G Rush (1991 Anaesthetic and nephrotoxic effects of Telazol in New Zealand white rabbits *Lab Anim Sci* **41** (5) 432 435

Bree M M , B J Cohen and S E Rowe (1972) Dissociative anaesthesia in dogs and primates *Lab Anim Sci* 22 (6 878 881

Bush M J A M Graves S J O'brien and D E Wild (1990 Dissociative anaesthesia in free ranging male koalas and selected marsupials in captivity *Australian Vet J* 67 (12) 449 451

Calderwood H W , A M Klide, B B Cohn, and L R Soma (1971) Cardiorespiratory effects of tiletamine in cats *Am J Vet Res* 32 (10) 1511 1515

Chen, G and C R Ensor (1968) 2 (Ethylamino) 2 (2 Thienyl) cyclohexanone HCl(CI-634) a taming incapacitating and anaesthetic agent for the cat *Am J Vet Res* 29 (4) 863 867

Colby D E and D T Sanford (1981) Blood pressure and heart and respiratory rates of cats under ketamine/ xylazine ketamine/acepromazine anaesthesia *Feline Pract* 11 (5) 19 24

Cornelius C E J Bishop, J Switzer and E A Rhode (1959) Serum and tissue transaminase activities in domestic animals *Cornell Vet* **49** (1) 116-125

Donaldson L L C J McGrath and C H Tracy (1989) Testing low doses of intravenous Telazol in canine practice *Vet Med* **84** (12) 1202-1207

Eucs, E F (1976) Telazol (CI-744) A new agent for chemical restraint and anaesthesia in nonhuman primates *Vet Med Small Anim Clin* 71 (6) 648

Fagella, M A G Michael and Aronsdan (1994) Evaluation of anaesthetic protocols for neutering 6 14 weeks old pups *J Am Vet med Ass* **205** (21) 308

Farina C and D Fonda (1991) Clinical use of a tiletamine zolazepam combination for general anaesthesia or cats *Veterinaria (Cremona)* **5** (4) 25-32 (Cited in *Vet Bull* (1992) **62** (8) 860)

Fieni, F and D Tainfurier (1993) The application of Tiles- for intravenous anaesthesia in dogs *Kleintierpraxis* 38 (2) 111-112 (Cited in *Vet Bull* **64** (7) 686)

Forsythe, D B , A J Payton, D Dixon P H Myers J A Clark and J R Snipe (1992) Evaluation of Telazol x lazine as an anaesthetic combination for use in Syrian hamsters *Lab Anim Sci* **42** (5) 497 502

Greere N M (1972) Metabolic effect of anaesthetics in *Modern Inhalation Anaesthetics* 1st ed Edited by Cheroweth M B Springer-Verlag, New York, N Y p 271 (Cited in Peshin P K and Kumar (1983) Haemocytological and biochemical effects of xylazine in buffaloes *Indian Vet J* **60** (12) 981-986)

Harvey, J , H Falsetti, P Cooper and D Downing 1983 Auscultatory indirect measurement of blood pressure in dogs *Lab Anim Sci* **33** (4) 370-372

Haskins S C R L Peiffer, Jr and C M Stowe (1975) A clinical comparison of CT 1341 ketamine and xylazine in cats *Am J Vet Res* **36** (10) 1537 1543

Hatch R C J D Clark A D Jernigan and C H Tracy 1988 Searching for a safe effective antagonist to Telazo overdose *Vet Med* **83** (1) 112 117

Helleyer, P W W Muir J A E Hubbell and J Sally (1989 Cardiorespiratory effects of the intravenous administration of tiletamine zolazepam to dogs *Vet Surg* 18 (2) 160 165 (Cited in *Vet Bull* 1990)

Hubbell J A E R M Bednarski and W W Muir (1989) X lazine and tiletamine-zolazepam anaesthesia in horses *Am J Vet Res* 50 (5) 737-742

Humason, G L (1979) *Animal Tissue Techniques* 4th ed W H Freeman and Company San Francisco p 129

Jacobson E R (1983) Haematologic and serum chemical effects of a ketamine/xylazine combination when used for immobilizing springbok *J Am vet med Ass* 183 (11 1260-1262

King M J B C R Bertram and H P Hamilton (1977) Tiletamine and zolazepam for immobilization of wild lions and leopards *J Amm vet med Ass* 171 (9) 894-898

Klide A M H W Calderwood and L R Soma (1975 Cardiopulmonary effects of xylazine in dogs *Am J Vet Res* 36 (7) 931 935

Ko H C J C J Thurmon, J G Benson and J W Tranquil (1993) An alternative drug combination for use in declawing and castrating cats *Vet Med* 88 (11) 106

Krahwinkel Jr D J (1970) The use of tiletamine hydrochloride as an incapacitating agent for a lion *J Am vet med Ass* 157 (5) 622 623

Kristensen T and C G Nielson (1993) Injection anaesthesia in cats new options in anaesthesia and pain control in cats and dogs) *Dansk Veterinaertidsskrift* **76** (22 9?3 (Cited in *Vet Bull* (1994) **64** (4) 990)

Kumar A and J C Thurmon (1977) A note on pharmacological effects of diazepam with and without pre administration of atropine in goats *Indian J Anim Sci* **47** (2 99-103

Lagutchik, M S A J Januszkiewicz K T Dodd and D G Martin (1991 Cardiopulmonary effects of a tiletamine zolazepam combination in sheep *Am J Vet Res* 52 (9 1441 -47

Lele C M and A P Bhokre (1985) Evaluation of xylazine as an anaesthetic agent in combination with certain preanaesthetic drugs in dogs I Respiratory rate heartrate and temperature *Indian vet J* **62** (8) 675 682

Lendl C H J Heur T Trillig, U Matis and T W Erhard (1991 Comparative investigations of four anasethetic methods in cats *J Vet Anaes* Special Supplement 201-2 3 (Cited in *Vet Bull* (1993) **63**(10) 1021)

Lin H C , J C Thurmon G J Benson, W J Tranquilli and W A Olson (1989) The haemodynamic response of calves to tiletamine zolazepam anaesthesia *Vet Surg* 18 (4 328 3 - (Cited in *Vet Bull* (1990) **60** (2) 184

Lin H C , J C Thurmon W J Tranquilli G J Benson and W A Olson (1991) Haemodynamic response of calves to tiletamine-zolazepam-xylazine anaesthesia *Am J Vet Res* 52 (10) 1606-1610

Lin H C , J W Tyler, S S Wallace J C Thurmon and D F Wolfe (1992) Telazol and xylazine anaesthesia in sheep *Cornell Vet* **83** (2) 117-124

Lin H C S S Wallace J W Tyler, R L Robbins J C Thurmon and D F Wolfe (1994) Composition of tiletamine zolazepam-ketamine and tiletamine zolazepam-xylazine anaesthesia in sheep *Australian Vet J* **71** (8) 239 242

McCarthy J E C M Trim and D Ferguson (1990) Prolongation of anaesthesia with xylazine, ketamine and guaifenesin in horses 64 case (1986-1989) *J Anim vet med Ass* **197**(12 1646-1650

Malek M A D B Patil K Sukumaran R R Parsania and M P Patel 1988) Haematological and biochemical changes during visceral procaine blockade lumbar epidural and local infiltration anaesthesia in buffalo calves *Indian J Vet Surg* **9** (2) 107-110

Moens Y and F Fargetton (1990) A comparative study of medetomidine/ketamine and xylazine/ketamine anaesthesia in dogs *Vet Rec* **127** (23) 567 571

Muir W W R Skarda and D W Milne (1977) Evaluation of xylazine and ketamine hydrochloride for anaesthesia in horses *Am J Vet Res* **38**(2) 195 201

Muir W W R T Skarda and W Sheehan (1978) Evaluation of xylazine guaifenesin, and ketamine hydrochloride for restraint in horses *Am J Vet Res* 39 (8 127- 1278

Nowrouzian I , H F Schels, I Ghodsian and H Karimi 1981 Evaluation of the anaesthetic properties of ketamine xylazine/atropine combination in sheep *Vet Rec* 108 (16) 354 356

Pandey, S K I J Sharma and S K Tiwari (1991) Clinical and haematological response to diazepam ketamine anaesthesia in canine surgical patients *Indian J Vet Surg* 12 (2) 102 104

Peshin, P K and A Kumar (1983) Haemocytological and biochemical effects of xylazine in buffaloes *Indian Vet J* 60 (12) 981-986

Peshin, P K A Kumar and H Singh (1980) Cardiovascular respiratory haematologic and sedative effects of xylazine in dogs *Indian J Vet Surg* 1 (1) 12-17

Popilskis, S J , M C Oz P Gorman, A Florestal and D T Kohn (1991) Comparison of xylazine with tiletamine zolazepam (Telazol) and xylazine-ketamine anaesthesia in rabbits *Lab Anim Sci* 41 (1) 51-53

Purohit R C P W Mysinger and R W Redding (1981 Effects of xylazine and ketamine hydrochloride on the electroencephalogram and the electrocardiogram in the horse *Am J Vet Res* 42 (4) 615 619

Raptopoulos D and B M Q Weaver (1984) Observations following intravenous xylazine administration in steers *Vet Rec* 114 (23) 567-569

Schalm C W (1975) *Veterinary Haematology* Lea and Febiger Philadelphia, 3rd ed pp 39-40 & 52 66

Schobert E (1987) Telazol use in wild and exotic animals *Vet Med* 82 (10) 1080-1085

Schulz, T A and M E Fowler (1974) The effects of CI 744 in chinchillas, *Chinchilla villidera* (Laniger) *Lab Anim Sci* 24 (5) 810-812

Sharif M N I Chaudry, M Nawaz and M S Durani 1991 Xylazine as a sedative and general anaesthetic in buffaloes *Pakistan vet J* 11 (4) 182-186 (Cited in *Vet Bull* (1992), 62 (9) 980)

Short, C E (1987) *Principles and Practice of Veterinary Anaesthesia* Williams and Wilkins, Battimore U S A pp 22 & 165

Silverman, J M Huhndorf M Balk and G Slater (1983) Evaluation of a combination of tiletamine and zolazepam as an anaesthetic for laboratory rodents *Lab Anim. Sci* 33 (5) 457-460

Singh K I S N Sharma K K Mirakhur and S Singh 1991) Clinical and biochemical effects of diazepam ketamine combination anaesthesia in calves *Indian vet J* 68 (3 253 25-

Smith R D and C E Pettway (1975) Absence of sensitization to epinephrine induced cardiac arrhythmia and fibrillation in dogs and cats anaesthetized with CI 744 *Am J Vet Res* **36** (5) 695-698

Snedecor G W and W G Cochran (1967) *Statistical Methods* 6th ed Oxford and I B H Publishing Co Calcutta Bomba/ New Delhi

Stander P E and P Morkel (1991) Field immobilization of lions using dissociative anaesthetics in combination with sedatives *African J Ecol* **29** (2) 137 (Cited in *Vet Bull* (1992) **62** (4) 385-386)

Stephenson, J C D I Blevins and G J Christie (1978) Safety of Rompun/Ketaset combination in dogs a two year study *Vet Med /Small Anim Clin* **73** (3) 303 306

Thurmon, J C G J Benson, W J Tranquilli W A Olson and C H Tracy (1988) The anaesthetic and analgesic effects of Telazol and xylazine in pigs evaluating clinical trials *Vet Med* **83** (8) 841 845

Thurmon, J C H C Lin G J Benson W J Tranquilli and W A Olson (1989) Combining Telazol and xylazine for anaesthesia in calves *Vet Med* **84** (8) 824 8

Tiwari S K R Sharda and S K Yadav (1994) Clinical and haematobiochemical response to ketamine with diazepam and xylaxine premedication in dogs *Indian Vet J* 71 (9 943 945

Tracy C H C E Short and B C Clark (1988) Comparing the effects of intravenous and intramuscular administration of Telazol *Vet Med* 83 (1) 104 111

Vleet J F V and Alberts (1968) Evaluation of liver function tests and liver biopsy in experimental carbon tetrachloride intoxication and extrahepatic bile duct obstruction in the dog *Am J Vet Res* 29 (11 2119-2131

Ward G S D O Johnsen and C R Roberts (1974) The use of CI 744 as an anaesthetic for laboratory animals *Lab Anim Sci* 24 (5) 737-742

Waterman, A E (1983) Influence of premedication with xylazine on the distribution and metabolism of intramuscularly administered ketamine in cats *Res Vet Sci* 35 (3) 285

Wintrobe, M M (1961) *Clinical Haematology* Lea and Febiger Philadelphia 5th ed pp 361-362

GENERAL ANAESTHESIA IN DOGS WITH TILETAMINE - ZOLAZEPAM

By

K. RAJANKUTTY

ABSTRACT OF A THESIS

Submitted in partial fulfilment of the requirement for the degree

Doctor of Philosophy

Faculty of Veterinary and Animal Sciences

KERALA AGRICULTURAL UNIVERSITY

Department of Surgery

COLLEGE OF VETERINARY AND ANIMAL SCIENCES

MANNUTHY, THRISSUR

1995

ABSTRACT

The present study was undertaken to findout the efficacy of tiletamine-zolazepam alone and with xylazine premedication for anaesthesia in dogs and to evaluate the systemic changes consequent on the administration of these drugs The experimental study was conducted on 36 adult non descript dogs of either sex The animals were randomly divided into two groups, (Group I and II) consisting of 18 animals each Each group was further divided into three subgroups viz A B and C consisting of six animals each

Atropine sulphate (0 04 mg/kg bodyweight) was administered IM 15 minutes prior to the administration of the experimental drugs in all the dogs Tiletamine zolazepam (T Z) combination was administered IM at the rate of 5 mg 10 mg and 15 mg/kg bodyweight in the subgroups IA, IB and IC respectively Xylazine at the rate of 0 5 mg/kg bodyweight and 15 min later T Z combination at the rate of 5 mg, 10 mg and 15 mg/kg bodyweight were administered IM in the subgroups IIA IIB and IIC respectively

The induction time was 6 17 ± 1 01 min 4 33 ± 0 21 min and 4 33 ± 0 49 min in subgroups IA IB and IC respectively and 3 33 ± 0 62 min 3.7 ± 0 48 min and 2 83 ± 0 54 min in subgroups IIA IIB and IIC respectively Increase in the dose of T Z

reduced the induction time and premedication with xylazine further reduced the induction time and induction was smooth

The onset of effect of tiletamine zolazepam was characterised by the winking of eyes yawning, licking and protrusion of tongue The eyes remained open and pupil were slightly dilated The palpebral and pedal reflexes and swallowing movements were not abolished Salivation was scant in both the groups

In the animals of Group II the eyes were partially closed and palpebral and pedal reflexes were abolished but the swallowing movements were not Protrusion of tongue though present, was not to the extent that was observed in the animals of Group I Rhythmic side to side head movements were noticed during induction in all the animals of Group I but not in animals of Group II

The duration of anaesthesia was 33 67 ± 5 88 min 57 83 ± 6 7 min and 89 00 ± 2 86 min in subgroups IA IB and IC respectively whereas it was for 49 67 ± 6 643 min 105 17 ± 10 31 min and 125 83 ± 10 78 min in subgroups IIA IIB and IIC respectively An increase in the dose of tiletamine zolazepam had prolonged the duration of anaesthesia and premedication with xylazine produced still longer duration of anaesthesia

The jaw musculature maintained the tonus with the lower doses of tiletamine-zolazepam, but at 15 mg/kg bodyweight the jaw muscles though not fully relaxed, permitted endotracheal intubation Administration of tiletamine-zolazepam with xylazine resulted in relaxation of the jaw muscles and permitted endotracheal intubation Relaxation of the abdominal muscles were moderate to good when tiletamine zolazepam alone was administered whereas it was excellent with xylazine premedication

Administration of tiletamine-zolazepam alone was found insufficient for carrying out surgical procedures, but with xylazine premedication muscle relaxation and analgesia was satisfactory

The recovery time was 111 50 ± 14 53 min 116 50 ± 10 46 min and 180 33 ± 10 57 min in subgroups IA IB and IC respectively and it was 160 00 ± 17 70 min 180 00 ± 14 94 min and 181 06 ± 12 82 min in subgroups IIA IIB and IIC respectively Increase in the dose of tiletamine-zolazepam had delayed recovery and xylazine premedication delayed it still further During recovery, paddling and vocalization were common in dogs of Group I but not in dogs of Group II

Reduction in rectal temperature was observed only in animals of subgroups IB and IC and in all the animals of Group II Marked increase in pulse rate was observed in Group

than in Group II Respiration rate was decreased in both the groups

A mild increase in diastolic pressure was observed in Group I The systolic and diastolic pressures were seen decreased in Group II The changes in the coagulation time of blood was within the normal limits in both the groups

Increase in heart rate with depression of T wave biphasic T-wave and spiking of T wave were the changes in electrocardiogram But the changes were corrected spontaneously

There was slight decrease in the erythrocyte sedimentation rate in animals of Group I but there was no change in Group II

Reduction in the packed cell volume was observed in both the groups but it was more, after xylazine premedication

Slight decrease in haemoglobin concentration was noticed in subgroup IC But there was no change in Group II

Decrease in total erythrocyte count was noticed in both the groups and the decrease was more when premedicated with xylazine

The total leukocyte count was seen increased in subgroup IA ard IB but it was seen decreased in subgroup IC but there was no change in Group II

Decrease in lymphocyte count with increase in neutrophil count was observed in subgroups IA and IIA In subgroups IB and IC there were increase in lymphocyte count with decrease in neutrophil count but in subgroups IIB and IIC a decrease or no alteration in the count of lymphocytes was observed Monocyte and eosinophil counts were increased and the basophil count remained insignificant

There was marked increase in the serum glucose value following the the administration of tiletamine zolazepam ard with xylazine premedication the increase was more

No significant change was observed in the serum electrolytes (Na K and Cl), total serum protein content and serum urea nitrogen value in both the groups

Slight increase in serum aspartate aminotransferase (AST) and serum alanine aminotransferase (ALT) values were observed in Group I ard in Group II there was increase in AST value but the ALT value decreased initially and was followed by an increase

Histopathological examination of liver revealed cloudy swelling and mild fatty changes and kidney revealed cystic dilation of the renal tubules along with focal areas of nephrosis