Comparative Studies on the Effect of Xylazine and Ketamine Alone and in Combination as General Anaesthetic in Caprine

THESIS

SUBMITTED TO THE

RAJENDRA AGRICULTURAL UNIVERSITY

PUSA (SAMASTIPUR) BIHAR

(FACULTY OF POST-GRADUATE STUDIES)

In partial fulfilment of the requirement

FOR THE DEGREE OF

Master of Veterinary Science

IN

(SURGERY AND RADIOLOGY)

By

Anil Kumar Lugun

Reg. No. - M/VSR/61/2001-2002

Department of Veterinary Surgery and Radiology

BIHAR VETERINARY COLLEGE

PATNA (BIHAR)

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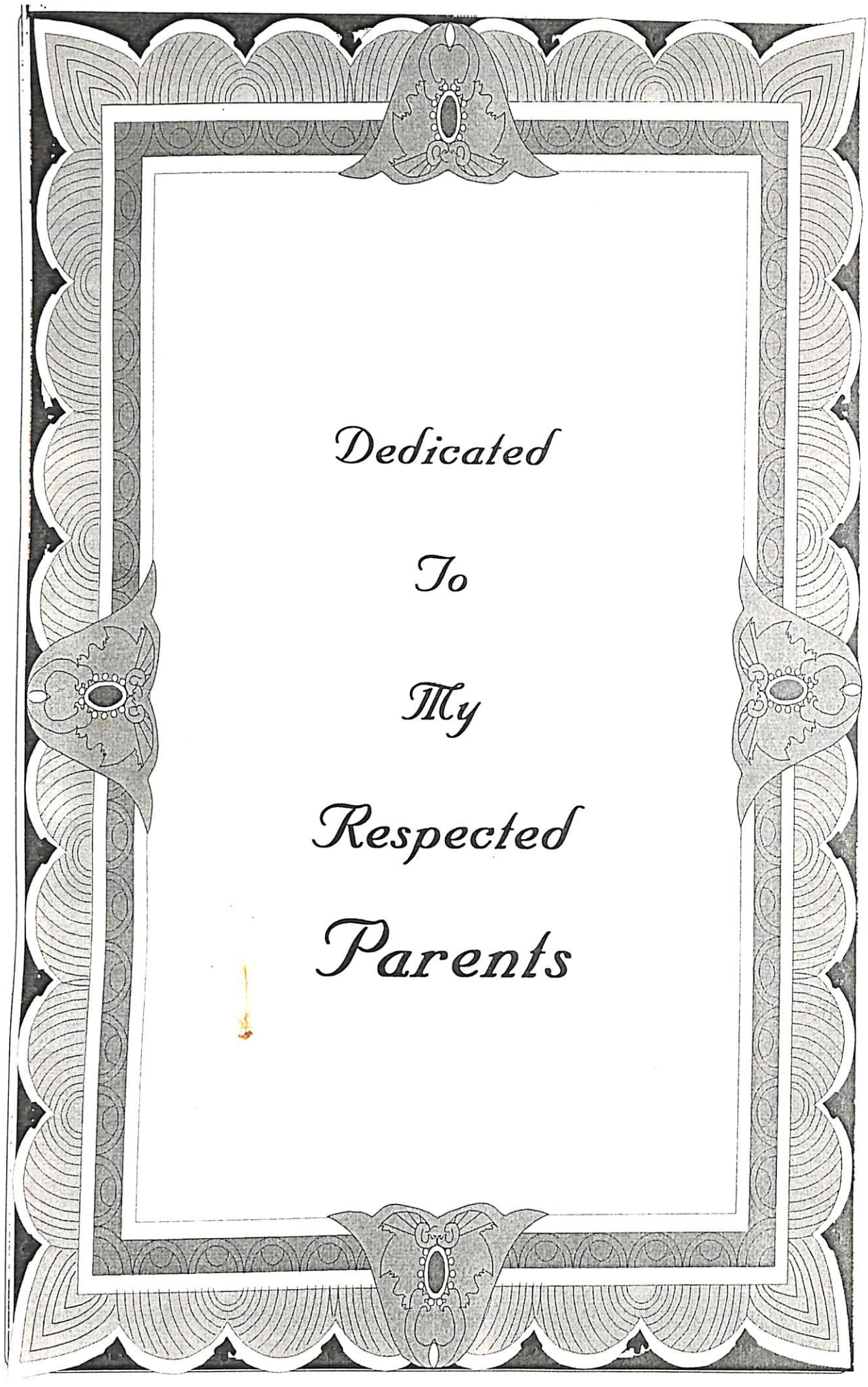
Dedicated
To
My
Respected
Parents

DEPARTMENT OF VETERINARY SURGERY AND RADIOLOGY
BIHAR VETERINARY COLLEGE, PATNA-14
RAJENDRA AGRICULTURAL UNIVERSITY
PUSA (SAMASTIPUR) , BIHAR.

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CERTIFICATE-I

This is to certify that thesis entitled ***"Comparative studies on the effect of xylazine and ketamine alone and in combination as general anaesthetic in caprine."*** submitted in partial fulfilment of the requirements for the Degree of **Master of Veterinary Science (Surgery and Radiology)** of the Faculty of post-graduate studies, Rajendra Agricultural University, Pusa, Samastipur, Bihar is the record of bonafide research work carried out by **Dr. Anil Kumar Lugun**, Registration no. M/VSR/61/2001-2002, under my supervision and guidance. No part of the thesis has been submitted for any other degree or diploma.

It is further certified that the assistance and help received during the course of this investigation and preparation of the thesis have been fully acknowledged.

31/3/04

(*S.P. Sharma*)

Major Advisor

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CERTIFICATE-II

We, the undersigned members of the Advisory Committee of **Dr. Anil Kumar Lugun**, Registration No. M/VSR/61/2001-2002, a candidate for the Degree of Master of Veterinary Science with Major in **Veterinary Surgery and Radiology** have gone through the manuscript of the thesis and agree that the thesis entitled ***"Comparative studies on the effect of xylazine and ketamine alone and in combination as general anaesthetic in caprine "*** may be submitted by **Dr. Anil Kumar Lugun**, in partial fulfilment of the requirements for the degree.

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This is to certify that the thesis entitled ***"Comparative studies on the effect of xylazine and ketamine alone and in combination as general anaesthetic in caprine."*** submitted by **Dr. Anil Kumar Lugun**, Registration No. M/VSR/61/2001-2002, in partial fulfilment of the requirements for the Degree of **Master of Veterinary Science (Surgery and Radiology)** of the Faculty of Post-Graduate studies, Rajendra Agricultural University, Pusa, Samastipur, Bihar, was examined and approved on ....4/6/.... 2004.

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Anil Kr Lugun

Anil Kumar Lugun

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CONTENTS

CHAPTER - 1

INTRODUCTION

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Major advances in the field of anaesthesiology as the result of development of new anaesthetics and equipments have been marked during the last decades. The development of newer surgical techniques and diagnostic methods in all phases of veterinary practice and their extension to old and chronic ill patients have demanded from the clinicians for the new anaesthetic approaches. Anaesthetic is the drug, indeed the miracle for surgery which relieves pain in both men and animals and it has enabled the surgeons to save millions of lives.

A variety of newer drugs has been added to the veterinary armamentarium allowing the safer management of an increasing number of species of animals. Owing to the anatomical and physiological differences as compared with other species, the goats require special attention alike bovine when general anaesthesia is being considered. Though, majority of surgical procedures are performed under local and regional anaesthesia but in certain surgical situations general anaesthesia becomes mandatory.

It is explicit therefore that like cattle, goats are also unsuitable subjects for general anaesthesia. However, in recent past caprine anaesthesia has received more attention but the endeavours could not make much headway towards obtaining satisfactory results (Kelawala and Parsania, 1992) and thus anaesthesia is still a challenging problem for this species.

Keeping these aspects in view, an attempt has been made to introduce xylazine and ketamine hydrochloride alone and in combination as general anaesthesia in the armamentarium of caprine anaesthesia α_2 agonist like xylazine has been under active consideration for general anaesthesia.

Xylazine is a non-narcotic α_2-adrenergic agonist, highly active agent with sedative, central muscle relaxant and analgesic properties. Xylazine is presently used as sedative agent by parenteral administration. In the present study xylazine has also been selected for administration by intramuscular route as a general anaesthetic. Xylazine prevents nerve impulse transmission. It exerts its systemic effects. It produces longer duration of analgesia and there is ataxia of lesser degree. Longer duration of analgesia may be helpful in providing analgesic umbrella to the animal during post operative period, facilitating post surgical management of the animal. It induces variable degree of sedation after intramuscular administration in animal.

To overcome the side effects of xylazine, an attempt has been made to explore the practical usefulness of adding Ketamine hydrochloride. Ketamine hydrochloride is a dissociative anaesthetic, rapid acting non-narcotic and non-barbiturate agent. Ketamine, an analogue of phencyclidine group has been used successfully alone and in combination with other drugs by few workers in caprine (Kumar, 1976, Kumar and Thurmon, 1977, Kumar *et al.*, 1983, Kumar *et al.,* 1986). This agent has numerous useful properties and it can be very safely used in aged, dehydrated, anaemic and those with chronic lung diseases. Ketamine HCl is an agent/drug of choice for short surgical procedures as dehorning, castration and ear-tattooing (Gary L. Kellar and David H. Bauman 1978). It can also be used for drainage of an abscess, wound debridement, orthopaedic manipulation, dilatation of a urinary stricture or for most abdominal procedures. Ketcham, 1990 had mentioned that the drug was metabolized in the liver and it was not contra indicated even in liver disease. Administration of this drug has been

associated with inadequate muscle relaxation, convulsion, rough emergence and excessive salivation.

So, it has become essential to evolve such type of anaesthetic method for surgical procedures in goats which are safe as well as effective and could replace the existing traditional methods having associated risks. The result of the present study will explore the practical feasibilities and their suitability of application in caprine. The clinico-biochemical findings may pave the way for its application in the patients having chance of poor surgical risks and conventional methods are contraindicated. It would also help a lot to field veterinarians who are often confronted with situations in which surgery is urgently required but there is lack of trained anaesthetist.

Therefore, in the present study, xylazine and ketamine alone and in combination were evaluated as general anaesthetics in caprine with following objectives :

(i) To evaluate the use of xylazine alone as general anaesthesia in goats.

(ii) To evaluate the use of ketamine alone as general anaesthesia in goats.

(iii) To compare the combination of xylazine and ketamine as general anaesthesia in goats from the above mentioned anaesthetic agents.

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CHAPTER - II

REVIEW OF LITERATURE

REVIEW OF LITERATURE

Hoeppner and Short (1971) advocated that ketamine has a rapid action, it is safe and satisfactory and could be used for a wide variety of diagnostic and surgical procedures.

Humphery (1971) conducted extensive clinical trials with ketamine hydrochloride and it was safe and effective general anaesthesia for canine surgery when it was used in dose rate of 20 mg/kg b.wt.

Strub (1971) studied that the optimal anaesthetic dose of xylazine in sheep was injected 3 mg/kg b.wt. by i/m route. The maximum effect occurred in 15 minutes and lasted upto 45 minutes after injection. Good results were obtained in 59 sheep anaesthetized for collection of C.S.F., lung biopsy sampling, foot rot, laparotomy and caesarean section. Some of the lambs born by caesarean section died soon afterwards, and a lower dose (0.15 mg/kg) was recommended for this operation.

Amend *et al.,* (1972) studied the concurrent use of xylazine (i/m) followed by ketamine hydrochloride (i/m) in cats. They observed that xylazine eliminated muscular tonicity, prolonged the duration of analgesia at low doses of anaesthetic, and provided sedation of sufficient duration to assure quite recovery.

Berlinger and Lakatos (1972) reported that ketamine hydrochloride is suitable for short, simple surgical operations at a dose of 20 mg/kg i/m in cats. Anaesthesia was achieved after 3-4 minutes and lasts about 20 minutes. They suggested that ketamine was contraindicated for cats suspected of circulatory disorders, since it increased blood pressure, heart rate and induced occasional extrasystole.

De-Young (1972) discussed that dissociative anaesthetic agents had the potential to revolutionize the anaesthetic management of the dog and cat. They could become an integral part of a regimen of balanced anaesthesia in veterinary medicine. The dissociative state produced by these agents were characterized by muscle rigidity and the presence of many reflexes (e.g. swallowing, laryngeal and occular) which were normally absent when general anaesthetic agents were used. The cardiovascular and respiratory effects of the dissociative anaesthetic agents and their application in clinical practices were also discussed.

Hopkins (1972) observed that intramuscular administration of a small dose of xylazine produces rapid onset of dose dependent sedation, analgesia and muscle relaxation in cattle. These characteristics of xylazine action and the absence of serious side effects should make it a valuable method of chemical restrin for cattle.

Thurmon *et al.* (1973) demonstrated that ketamine hydrochloride rapidly immobilized sheep when given i/v or i/m. Pretreatment of sheep with atropine sulphate and acepromazine prevented excessive salivation and increased the degree of muscular relaxation and duration of analgesia. The duration and degree of analgesia obtained at the dosages used (22 to 44 mg/kg) were adequate for short surgical and diagnostic procedures. The recovery was smooth and rapid.

Chiasson *et al.* (1973) reported that i/m injection of ketamine HCl in White Leghorn Cockerels produced rapid atrophic effects in the adrenal glands. Signs of recovery were recorded 5 days after injection of the drug.

Oeppert (1973) reported that ketamine and xylazine alone or when combined in various proportions in cats was adequate for minor surgery. For

further sedation subsequent injection of a half dose was sufficient. The respiratory frequency and volume was decreased, blood pressure increased and pulse rate was decreased.

Ivankovitch *et al.* (1974) did extensive work on ketamine hydrochloride and reported that apart from its normal analgesic effect it has a cardiovascular stimulant effect and therefore a very safe anaesthetic agent under various adverse situations.

Kumar and Thurman (1974) reported a significant increase in blood glucose level and in serum glutamic oxalacetic transaminase (SGOT) activity. The increased values returned to preadministration values in 72 hours.

Lanning and Harmel (1975) reported that the ventilatory response to hypoxia was not inhibited by ketamine. On the contrary it was observed that in response to hypoxic changes ketamine stimulated the respiratory centres.

Mottelib and El-Gindi (1975) in their studies on buffaloes tranquilized by Rompun 'Bayer' observed hyperthermia reduced respiratory and pulse rate. Urea nitrogen, bilirubin and blood creatinine levels rose. The blood iron content was decreased.

Kumar *et al.* (1976) reported xylazine in combination with ketamine showed increased skeletal muscle relaxation and duration of analgesia in domestic goats undergone a variety of surgical procedures. Salivation was moderate in all goats. Animals given ketamine anaesthesia maintained laryngeal and pharyngeal reflexes.

Kumar and Singh (1976) reported xylazine as immobilizing agent in cattle at 0.1 mg/kg by i/m administration. Surgical operations varying from 22-70 minutes duration were performed. The recovery was smooth and

uncomplicated. The respiratory and heart rate were reduced at maximal sedation. Total erythrocytes, leucocytes and haemoglobin concentration were reduced at maximal sedation, whereas, ESR increased. Neutrophilia with corresponding lymphocytopenia was also observed. Xylazine increased blood glucose, but this effect lasted for only 48 hours.

Shokry *et al.* (1976) used xylazine 0.1 and 0.3 mg/kg in sheep. They studied serum glutamic oxaloacetic transminase, serum lactate dehydrogenase, serum alkaline phosphate, cholesterol, total bilirubin, urea, uric acid, glucose, total protein, albumin, Ca, inorganic phosphorus K, Na, and Cl. There was only hyperglycaemia after xylazine administration.

Aziz and Martin (1978) studied that xylazine had local anaesthetic effect and produced analgesia probably by stimulation of α-2 adreno-ceptors in spinal cord and CNS, thereby inhibit the release of neurotransmitters and decreasing neuronal activity.

Keller and Bauman (1978) found that ketamine was the agent of choice for short surgical procedures which produced moderate anaesthesia with reasonable recovery time in goats. At the dose level used, no fasting was required. For prolonged surgery combination of ketamine and xylazine was suitable, it produced deep state of anaesthesia and good analgesia for periods ranging from 50-85 minutes.

Kumar and Singh (1978) reported the effect of xylazine @ 2.5 mg/kg i/m used in minor surgery under local procaine anaesthesia in horses. Sedation lasted for about 30 minutes in control and 40 minutes in surgical cases. Immobilization was achieved in about 15 minutes after administration. There was a slight decrease in blood cell counts and haemoglobin

concentration and a slight increase in blood sugar at the time of maximum sedation in all the cases.

Lin *et al.* (1978) reported that the hypothermia produced by ketamine alone may be due to decreased heat production as well as increased heat loss secondary to cutaneous vasodilation.

Campbell *et al.* (1979) observed the haemodynamic effects of sedative level doses of xylazine in five calves. These effect included immediately and prolonged reductions in heart rate, cardiac output arterial blood pressure and left ventricular dp/dt max. The results indicated that a depressed myocardium results from xylazine administration. Sedation by xylazine is produced in cattle at a lesser dose as compared to the dose required for sedation in other species.

Eichner *et al.* (1979) reported that intravenous administration of xylazine in ten beef cattle (0.2 mg/kg b.wt) resulted in rapid onset (<15 minutes) of hyper plasma glucose values increased to 195 ± 15 mg/dl and 305 ± 10 mg/dl at 15 minutes and 3 hrs respectively. Concomitantly plasma insulin concentration dropped from 23 ± 2 μU/ml before xylazine to 5.8 ± 0.7 μU/ml and 2.4 ± 0.3 μU/ml at 15 minutes and 3 hrs respectively. Plasma urea nitrogen was significantly ($P<0.01$) increased within 3 hrs of xylazine administration (6.7 ± mg/dl vs 11.4 ± 0.7 mg/dl).

Kumar *et al.* (1979) observed the combination effect of ketamine and xylazine in dogs. The i/m administration of xylazine at the rate of 0.22 mg/kg and ketamine 10 mg/kg with and without preadministration of atropine at a dosage of 0.65 mg produced good muscle relaxation and analgesia lasting from 29.65 ± 1.25 minutes to 36.55 ± 1.45 minutes. It permitted successful completion of variety of surgical procedures. The

supplemental increments with ketamine at the rate of 2-4 mg/kg prolonged the duration of anaesthesia by 14-22 minutes. The animals recovered in 90.2 ± 2.50 to 110.0 ± 2.75 minutes from the initial administration of ketamine. Supplemental increments with ketamine prolonged the recovery by 20-25 minutes. Rectal temperature, heart rate and respiratory rate were mildly decreased after ketamine and xylazine anaesthesia. Transient changes in haemocytological and glucose were observed.

Kumar and Singh (1979) observed that ketamine at 11 mg/kg i/m preceded by xylazine at 0.22 mg/kg i/m in calves produced good surgical anaesthesia lasting for 40-45 minutes. Different surgical procedures were carried out. There was a slight reduction in respiration, heart rate and rectal temperature during surgical anaesthesia. Recovery was smooth and uncomplicated, transient changes in erythrocytes, leucocytes, haematocrit, haemoglobin, Na K, Cl and glucose values were compensated in 48 hours. The combination of xylazine and ketamine was found satisfactory in paediatric bovine surgery.

Kumar and Thurmon (1979) observed marginal alteration in the creatinine levels in goats after administration of xylazine. These light variations were probably inconsequential.

Kumar and Thurmon (1979) reported that ketamine stimulated the autonomic nervous system and produced tachycardia and increased blood pressure in goats. Xylazine supresses the autonomic nervous system so it was used in combination with ketamine 0.22 mg/kg intramuscularly or intravenously to examine its effect on different concentrations of ketamine. They observed that the combination of drug given intravenously produced

satisfactory anaesthesia in goats. Atropine was used to control excessive salivation.

Kumar and Thurmon (1979) reported after intramuscular administration of xylazine reduced the rate of breathing, without affecting mean arterial blood pressure and rectal temperature. Preadministration of atropine did not affect the depth and pattern of respiration, but it increased heart rate. Glucose level increased at maximum depth of sedation. The blood changes returned to normal after 24-72 hours. Xylazine was well tolerated and the sedation was rapid in onset lasted for about 30 minutes. Recovery was uneventful.

Amer and Misk (1980) reported that the i/m injection of xylazine at 0.2 mg/kg body weight in six female goats was followed by an increase of glucose urea nitrogen and cholesterol levels and a decrease of chloride in blood serum and cerebrospinal fluid.

Knight (1980) reported that α2-agonists like xylazine, detomidine and medetomidine are centrally acting, non narcotic analgesic with sedative, myorelaxant and local anaesthetic properties.

Ponder and Clark (1980) reported that xylazine administration in cat resulted in reduced basal metabolic rate and muscle activity on the one hand and depression of thermoregulation on the other hand. Both these effects may act together to result in hypothermia.

Brockman (1981) reported that glucose metabolism subsequent to xylazine given i/v at the dose rate of 0.16 mg/kg body weight on adult crossbred sheep. Xylazine caused a significant rise in glucose concentrations. The peak concentrations occurred at 30 minutes but after 80 minutes glucose was still significantly elevated. Glucagon concentration

were significantly elevated at 5 and 15 minutes after injection. At 30 minutes glucagon was not significantly elevated and by 120 minutes it was significantly depressed. Insulin concentration were significantly depressed for 30 minutes after xylazine administration.

Hsu (1981) observed that central nervous system depressant effect of xylazine in mice and newly hatched chickens. Xylazine was given at the dose rate of 3 to 30 mg/kg body weight intraperitoneally. He observed that xylazine induced CNS depression is mediated by α-2 adrenergic receptors. This study further suggested that the use of yohimbin as an antagonist itself induced depression.

Ramakrishna *et al.* (1981) observed a significant increase in blood glucose and serum glutamine oxaloacetic transminase in buffalo calves after administration of ketamine anaesthesia. There was no significant variation in total proteins, albumin, glubulin, serum glutamic transaminase and alkaline phosphatase concentrations.

Waterman (1981) observed that respiratory and pulse rates decreased after xylazine administration, but rose again when the ketamine was given in calves. Bradycardia was not seen when the two drugs were given together. Muscle relaxation was good and recovery in all cases was smooth.

Muggaberg and Brockman (1982) observed a transient hyperglucagonaemia, hypoinsulinaemia and hyperglycaemia after administration of xylazine intravenously in sheep. Phentolamine prevented the xylazine-induced increase in the rate of appearance of glucose, and in concentration of glucose and glucagon in plasma. The xylazine-induced

effects on glucose metabolism and secretion by glucagon and insulin appeared to be mediated by the α-adrenoreceptors.

Samy *et al.* (1982) conducted experiment on mixture of ketamine (3 mg/kg) and xylazine (0.3 mg/kg) in sheep. Anaesthetic effect was obtained in small doses. The average anaesthetic period persisted for 75 minutes. Clinical study revealed increase in respiratory rate as well as decrease in pulse rate and body temperature. Study of haemogram revealed decreased level of erythrocytes, haemoglobin content, haematocrit and TLC. Lymphopenia, eosinopenia with subsequent rise in neutrophils were observed. The activities of the enzyme aspartate, alanine aminotransferase and alkaline phosphatase were increased. The BUN showed marked elevation. The Total serum protein calcium and inorganic phosphorus showed slight changes. The studied blood parameters returned to their pre-anaesthetic values 48 hours after anaesthetization.

Tantawy *et al.* (1982) in their studies on some clinical studies on Rompun (Bayer) in buffaloes observed increased body temperature, decrease in pulse rate respiration and ruminal movements after the animals were injected I/M with xylazine at 0.02, 0.03, 0.05 a 0.07 mg/kg body weight.

Wright (1982) reported that tachyphoea occurs due to a residual effect of ketamine. This is because of the fact that ketamine activates subcortical areas of C.N.S.

Ahuja (1983) reported that intrathecal administration of ketamine could produce analgesia, but its effect is of short duration and the magnitude is inconsistent one.

Kumar *et al.* (1983) reported that intramuscular administration of ketamine caused a significant increase in heart rate, blood pressure and

respiration rate in goats. Atropine with xylazine and ketamine caused an insignificant decrease in rectal temperature and did not modify the pattern or frequency or respiration in animals receiving ketamine. In goats given the combination of atropine xylaxine, and ketamine, pulse rate did not increase to the level induced by ketamine alone. This is probably due to the parasympathomimetic action of xylazine.

Peshin and Kumar (1983) studied the effect of the administration of xylazine i/m at 0.22 mg/kg b.wt. with and without prior administration of atropine at 0.04 mg/kg in buffaloes. Blood cytology and biochemistry were studied before 30 minutes, 24 hrs. and 72 hrs after administration. A slight decrease in total leucocytes, PCV and Hb concentration were observed. Significant increase in glucose 30 minutes after xylazine administration was detected while SGOT and SGPT slightly decreased. No significant change in serum electrolytes Na^+, K^+, Ca^+ and Cat was observed, minor changes were compensated in 24-72 hours.

Sharma *et al.* (1983) in their experiment on clinical evaluation of xylazine (rompun) as an anaesthetic for large animals, they observed that in horses even at higher dose anaesthesia was of poor quality and side effects including sweating, respiratory depressing and slowing of pulse.

Bion (1984) observed that intrathecal administration of ketamine alone did not produce motor block, but addition of adrenaline resulted in complete motor block and intensified the sensory blockade. Motor block persisted for the same duration in case of a surgical anaesthesia.

Livingston *et al.* (1984) reported that the decrease in body temperature, post epidural injection of xylazine was not only related to

central α-2 adrenergic mechanism but it was probably related to other mechanisms which depress CNS as well.

Islas *et al.* (1985) reported that epidural administration of ketamine produced potent analgesia without respiratory depression, urinary retention or together side effect like neurologic sequalae and discomfort.

Kumar *et al.* (1985) reported a significant increase in blood glucose level after administration of ketamine hydrochloride at the dose rate of 15 mg/kg body weight intramuscularly in goats.

Kuruishi *et al.* (1985) observed that post epidural administration of xylazine induced the analgesia through local anaesthetic action and α-2 adrenergic mechanism. These effects have been explained by the stimulation of α1 and α2 adrenoreceptors in the spinal cord and CNS. These actions results into the inhibition of the release of spinal substance P which counters the actions at the spinal level.

Singh *et al.* (1985) in their evaluation of xylazine-ketamine anaesthesia in buffaloes gave xylazine intramuscularly 0.22 mg/kg, followed 15 min. later by keamine intravenously (2mg/kg). This combination produced satisfactory anaesthesia of 30-45 minutes duration with good muscular relaxation. They also observed that no alteration in blood urea nitrogen, plasma concentrations of creatinine, total proteins and electrolytes.

Dhasmana *et al.* (1986) observed that intrathecal administration of ketamine (300 to 1500 μg/kg) produced a short lasting hypotension and bradycardia, Which may be due to inhibition of sympathetic out flow. When 5 mg/kg of ketamine was injected into the cerebral circulation it produced a rise in heart rate and blood pressure, probably through a cholinergic mechanism.

Kumar *et al.* (1986) reported that ketamine, a analogue of phencyclidine group has been used successfully alone and in combination with other drugs in goat. They also observed a slight salivation after administration of ketamine. The stimulation of post ganglionic termination of cholinergic fibres in the autonomic nervous system by ketamine may be the possible reason for salivation. Temperature and respiration remained unaffected but the heart rate was significantly increased upto 30 min. after administration of ketamine which was diclined to normal levels by 120 minutes.

Wyk and Berry (1986) observed that combination of ketamine 8 mg/kg and xylazine 3.2mg/kg produced effective immobilization in lions (Panthera leo) for 4 hrs. Ataxia and immobilization were induced with stable respiratory rate, heart rate and body temperature. They further reported that tolazoline effectively antagonized xylazine by i/v or i/m injection, resulting in a return to mobility within about 20 or 60 minutes respectively. Tolazoline also raised the respiratory rate. No death was reported during 97 immobilization of 76 lions.

Nolan *et al.* (1987) reported that the antinociceptive activity of i/v administration α-2 adrenorecptors agonists. Clonidine and xylazine was measured in sheep using thermal and mechanical pressure threshold defection systems. Antinociceptive activity for both forms of threshold stimuli exhibited by both the drugs. The antinociceptive effects were reversed by idazoxan (0.10 mg/kg i/v) but were not affected by naloxone at 0.2 mg/kg i/v indicating that these effects were mediated α-2 adreno-ceptors.

Ravat *et al.* (1987) reported that epidurally administered ketamine in doses of 30 mg. and more seen to provide adequate post operative analgesia,

while smaller doses might be effective in chronic pain syndromes. However in one plot study 30 mg. of epidural ketamine produced analgesia with sedative effects, which could be examined by vascular uptake from epidural space of systemic action.

Vicente *et al.* (1987) formulated anaesthetic regimes of ketamine plus xylazine i/m at doses of 5 mg plus 0.2 mg (I), 10 mg plus 0.2 mg (II) 10 mg plus 0.3 (III) and 10 mg plus 0.3 mg (IV) per kg of b.wt. in sheep. Rumenotomy was done after 24 hrs. of fasting and 12 hrs. without water. Rectal temperature, respiratory and heart rates palpebral, corneal and pedal reflexes, induction time, time of decubitus, muscular relaxation and time before ability to walk was observed. It was considered that the most satisfactory dosage was 10 mg plus 0.2 mg/kg.

Waterman *et al.* (1987) observed that intrathecally administered xylazine in experimental sheep showed its potent analgesic properties when used in the same manner. It is now clear that the use of α-2 agonists locally around the spinal cord offers the veterinary surgeons new possibilities for the provision of analgesia during and following surgery.

White *et al.* (1987) observed the effect of either xylazine (0.25 mg/kg) and ketamine (5.5 mg/kg) i/m or a mixture of xylazine (0.15 mg/kg) and ketamine (2.5 mg/kg) i/m in domesticated dromedary. Either drug used separately was suitable for sedation and analgesia, but the mixture of xylazine and ketamine was superior to either drugs used alone. Camels which received the combination had fewer effects on cardiac and respiratory stability and had satisfactory analgesia. In addition, they showed better muscle relaxation, less nervous system irritability and shorter recovery times than camels sedated with ketamine alone.

Angel and Langer (1988) reported that the hyperglycaemic effect might be due to an α-adrenergic inhibition of insulin released by stimulation of α_2-receptors in the pancreatic b-cells and to an increased glucose production in the liver in anaesthetized rats.

Hussain and Kumar (1988) in their experiment in tachyphylaxis to epidural anaesthesia in buffaloes. They observed no significant effect on acid base status, blood glucose, blood urea nitrogen, total serum proteins, creatinine and serum electrolytes (Na, K and Cl).

Le Blane *et al.* (1988) suggested that xylazine is an effective epidural analgesic in the horse. More prolonged duration of analgesia may result by use of injection with other α2-adrenergic agonists or narcotics combined with xylazine. Also, the addition of epinephrine appears to increase the duration of caudal epidural analgesia.

Waterman *et al.* (1988) reported that epidural administration of xylazine in sheep induces analgesia through a local anaesthetic action and an α-2 adrenergic mechanism.

Fayed *et al.* (1989) discussed the effect of i/v injection of xylazine in heifers under thermoneutral (18^0C, 42% humidity) of heat stress (33^0C, 63% humidity). Xylazine induced hypoinsulinaemia which was associated with hyperglycaemia. In thermoneutral group, serum glucose concentration increased from 65 to 105 mg/dl. Hyperglycaemia was on peak at 2 hrs. and remained high for 6 hrs. after xylazine administration. Xylazine had no effect on body temperature and respiration rate in thermoneutral condition, whereas it induced hyperthermia and suppressed respiration rate in heat stressed heifers. Pulse rate was slightly decreased in thermoneutral heifers and greatly decreased in the heat-stressed-heifers.

Skarda *et al.* (1989) elucidated that a dose dependent sedation has been observed in cow after caudal epidural administration of α-2 agonists (xylazine). They attributed this sedation action of xylazine due to its central α-2 adrenergic effects.

Vigo *et al.* (1989) observed good analgesia and rapid recovery with 1-2 mg/kg xylazine i/m as preanaesthetic, which was followed by 10-18 mg/kg ketamine intramuscularly in the pigs.

Jean *et al.* (1990) induced caudal epidural analgesia in cattle by administration of xylazine in the intercoccygeal space. It was observed an increase in rectal temperature but reason for the temperature change is unknown. Heart rate and respiratory rate were significantly decreased and the survival contractions were decreased markedly after the induction of anaesthesia.

Le Blanc and Cardon (1990) observed that xylazine epidural administered resulted in significant analgesia for various surgical procedure in the perineal region in horses. The duration of analgesia from single injection of epidural xylazine (0.17 to 0.22 mg/kg) was at least 3.5 hrs. None of the animal was ataxic during or after the treatment. Thus it concluded that prolonged regional analgesia provided by epidurally administered xylazine in horses, which were sufficient for clinical use.

Moens and Fregetton (1990) reported that systemic administration of xylazine / medetomidine with ketamine. It was convincingly demonstrated that the centrally stimulating effects of ketamine balance the depressive effects of α_2-agonist.

Skarda *et al.* (1990) reported that 0.05 mg/kg of xylazine injected into the caudal epidural space in cattle, induced analgesia, marked sedation,

ataxia and depression of respiratory, cardiovascular and ruminal motor function. They further elucidated that tolazoline administered intravenously @ 0.3 mg/kg reversed most rumen hypomotility and cardiopulmonary depression as well as undesirable pharmacologic effects of xylazine without significantly affecting analgesia and sedation.

Kelawala *et al.* (1991) on their studies on haematological and biochemical studies on ketamine, propofol and propofol administered diazepam i/v @ 0.75 mg/kg b.wt., after 10 minutes ketamine hydrochloride was administered i/v @ 1 mg/kg b.wt in group I. In group II diazepam as in group I, after 10 minutes propofol i/v @ 3.93 and 2.88 mg/kg b.wt. In group III same as in group II. Maintenance of anaesthesia done by i/v administration of ketamine hydrochloride @ 11 mg/kg b.wt. They observed insignificant decrease in Hb, PCV, TEC and TLC 10 minutes after diazepam administration in all the groups. A significant increase in blood glucose was recorded in all the groups. A non-significant increase in BUN upto 48 hours was seen in all the groups. A non-significant increase in serum creatinine was detected in group I and III.

Ramaswamy *et al.* (1991) reported that ketamine did not produce any cumulative or toxic effect in dogs. They observed that ketamine when administered in dogs, there is rough emergence, lack of adequate muscle relaxation and excessive salivation. These side effects could be overcome by ketamine-xylazine combination or ketamine-promazine combination.

Reddy *et al.* (1991) observed the effects of xylazine administered in two doses by i/m route in 14 to 16 months old crossbred calves. Pronounced sedative effect was observed at a dosage level of 0.3 mg/kg b.wt., while optimum effect was evident when 0.2 mg/kg b.wt. was administered. Slight

decrease in respiratory rate, heart rate, PCV, RBCs and WBCs was noticed with both the regimens.

Kelawala and Parsania (1992) studied ketamine, propofol and combination of propofol and ketamine as general anaesthesia in goats premedicated with diazepam. In the goats where ketamine was used as sole anaesthetic agent there was significant rise in heart rate, respiratory rate and decrease in body temp. There changes were insignificant in animals when propofol was and alone. However, heart rate & respiratory rate was significantly increased but body temp. revealed insignificant changes where combination of propofol and ketamine was employed.

Reibald *et al.* (1992) demonstrated that xylazine administered epidurally along with lignocaine in cattle produced analgesia of quicker onset that xylazine alone and of longer duration than either agent given alone.

Skarda and Muir (1992) reported that epidural administration of xylazine in horses and cattle can produce significantly longer duration of analgesia as compared to lignocaine administered epidurally.

Balakishan and Rao (1993) studied the effect of epidural administration of xylazine and lignocaine hydrochloride in buffalo calves. Caudal epidural analgesia was obtained with 2% xylazine (0.05 mg/kg and 0.07 mg/kg and lignocaine hydrochloride 0.05 ml/kg) given into first intercoecygeal space. It was concluded that xylazine produced prolonged analgesia and sedation with better maintenance of hind limb strength than lignocaine hydrochloride.

More *et al.* (1993) evaluated the efficacy of diazepam-xylazine-ketamine anaesthesia in calves of 6-12 months of age. Diazepam was

administered i/m 0.25 mg/kg 15 minutes prior to xylazine-ketamine mixture. Ketamine was administered i/v at the dose rate of 1,2 and 3 mg/kg in combination with xylazine (0.04 mg/kg) in group I, II and III respectively. Hyperglycaemia with non-significant changes in serum urea nitrogen, a slight reduction in TEC, Hb and slight decrease in TLC and PCV at maximum depth of anaesthesia were evidenced. DLC revealed significant neutrophilia with corresponding lymphocytopenia in animals of group II only.

Aithal *et al.* (1994) reported that ketamine not only reduced the cardiovascular depressant effects of epidural xylazine but also increased the extent of analgesia in goat, when employed epidurally.

Raidurg and Ranganath (1994) demonstrated that xylazine @ 0.05 mg/kg was given epidurally in calves provided satisfactory regional analgesia with desired level of sedation and the animal remained in the standing position. However, animal became recumbent after epidural administration of xylazine @ 0.1 mg/kg and exhibited marked salivation and vocalization. The effect of xylazine @ 0.05 mg/kg was less pronounced as compared to 0.1 mg/kg in terms of clinical parameters like rectal temperature, heart rate, arterial blood pressure and ruminal motility. It is concluded xylazine @ 0.05 mg/kg is best suitable for the use as an epidural analgesic in calves.

Rehage *et al.* (1994) observed that epidural administration of xylazine in cattle cause dose dependent cardiopulmonary depression. This was exhibited by significant decrease in heart rate, respiratory rate and arterial blood pressure.

Ekka *et al.* (1996) used ketamine hydrochloride 12 mg/kg in atropinized goats. They observed uniform increase in pulse and respiration rate and no effect on body temperature. The duration of action was 45.33 + 1.20 min. when xylazine was added with ketamine there was significant fall in rectal temperature, satisfactory sedation and muscle relaxation. Hyperglycaemia was a feature of ketamine+xylazine, ketamine + promazine with slight increase in aspartate aminotransferase level.

Pandey *et al.* (1996) in their studies to determine the utility and safety of xylazine-ketamine combination with and without diazepam in horses reported that the induction of anaesthesia was smooth in animals of both the groups. The induction was 43 ± 3.32 seconds and 63.32 ± 4.60 seconds in group I and II respectively. The duration of anaesthesia was 9.46 ± 1.62 minutes in group I and 25 ± 1.62 minutes in group II.

Skarda and Muir (1996) demonstrated that xylazine administered epidurally @ 0.17 mg/kg, 0.25 mg/kg) in mares produced dose dependent cardio pulmonary depression, Post epidurally administered xylazine exhibited significant decrease in heart rate, respiration rate and arterial blood pressure and mild to moderate sedation.

Aithal *et al.* (1997) reported that epidural administration of xylazine @ 0.05 mg/kg cause dose dependent cardiopulmonary depression. Variable alterations in heart rate, respiratory rate, arterial blood pressure and mild to moderate sedation were observed after epidural administration of xylazine in goats.

Aithal *et al.* (1997) reported that even though ketamine possesses cardiostimulatory actions but it did not produce any significant change in the heart rate after epidural administration in goats. They conduced that the

lack of change in heart rate could be due to the small dose of ketamine used in their study.

Aithal *et al.* (1997) in their studies on epidural ketamine and xylazine for hindquarter surgery in ruminants on 35 clinical cases reported that the efficacy of epidural administration of ketamine at 2.5 mg/kg and xylazine at 0.05 mg/kg was examined in 18 goats, 16 cattle and one buffaloe that underwent various surgical procedures. The onset of analgesia was observed within 2 min. in goats and within 5 min in cattle. The duration of analgesia was 50 to 60 min.

Amarpal *et al.* (1997) observed that a mixture of xylazine @ 0.05 mg/kg and ketamine @ 100 mg administered lumbosacral epidurally in cow calves produced good analgesia of hind quarter without any alarming clinical side effects. Ketamine in combination with xylazine produced a longer duration of an anaesthesia in comparison to ketamine or xylazine alone, it might be due to synergistic interaction between ketamine and xylazine.

Kinjavdekar *et al.* (1997) observed that xylazine @ 0.05 mg/kg (2ml) and a combination of xylazine @ 0.05 mg/kg and ketamine @ 2.5 mg/kg (2ml) was administered epidurally at first lumbar in vertebral space in 10 adult goats. Marked reduction in heart rate, respiration rate, moderate analgesia, severe in coordination with standing posture mild sedation were recorded in xylazine treated animals. Reduction in heart rate, with lesser extent and duration, relatively less reduction in repiration rate, complete to moderated analgesia throughout the period of observation with recumbent posture mild sedation and salivation were observed in xylazine and ketamine treated animals. There was no change in the temperature in both the cases. It was concluded that ketamine and xylazine combination provided excellent

analgesia of flank,thorax,ventral abdomen and hind limbs, if used at the first lumbar epidural space without clinically evident side effects.

Amarpal *et al.* (1998) conducted the study on 12 adult dogs divided in groups A, B and C in which epidural administration respectively ketamine 2.5 mg/kg, pethedine 2 mg/kg and combination of ketamine 2.5 mg/kg and pethedine 2 mg/kg was done. Heart rate, respiration rate increased but no change in rectal temperature in all the groups. Mild to moderate analgesia complete in coordination of short duration were observed. Sedation was not appreciable in any of the groups.

Barbalia *et al.* (1998) conducted clinical and physiological studies on epidural use of lignocaine, ketamine or combination of lignocaine + xylazine @ 0.5 mg/kg, 1 mg/kg, and 0.5 mg/kg + 1 mg/kg respectively in goats. They observed better analgesia with respect to depth and degree as well as significant but transient decrease in heart rate which was compensated with 30 minutes after onset. Epidural injection of lignocaine in conjunction with ketamine in same syringe was superior and can be used in routine clinical practice.

Chitale *et al.* (1998) observed the use of ketamine for induction of anaesthesia after premedication with diazepam – xylazine (Gr. A), diazepam-medetomide (Gr. B), diazepam-romifidine (Gr.C) and diazepam alone (Gr.D) in atropinised goats. Slight and transient increase in heart rate and rectal temperature was seen after administration of α-2 agonist. Heart rate increased further but temperature decreased after ketamine administration. It was maximum in the animal of group C. Respiration rate remained within normal range after premedication in all the groups.

Kinjavdekar (1998) Observed that epidural/intrathecal administration of α-2 agonists cause dose dependent cardiopulmonary depression. The heart rate, respiration rate and arterial pressure were significantly decreased after epidural administration of xylazine in goats.

Pratap *et al.* (1998) observed the effects of epidural administration of xylazine @ 0.1 mg/kg body weight in buffalo calves. There was significant reduction in heart rate and respiration rate for a short duration and fall in rectal temperature was noted for a longer duration. Onset of analgesia was within 2 to 12 minutes in all the animals and excellent analgesia of tail, perineum, hind limb, flank and ventral abdomen was observed for 60 to 120 minutes. Sedation was moderate in all animals and they remained in standing position throughout the period of observation. Adequate muscle relaxation was felt. Analgesia was found sufficient for surgical intervention of hind quarters in buffalo-calves.

Varshney (1998) conducted experiments to evaluate the clinical efficacy of xylazine hydrochloride in six healthy ponies. Xylazine hydrochloride @ 0.5 and 1.1 mg/kg body weight was administered intravenously in group A and B respectively consisting of three animals in each. Time of onset of analgesia varied from 1.0 to 3.5 minutes of on I/V administration of xylazine hydrochloride. Rectal temperature, pulse rate and respiration rate lowered after 30 minutes of xylazine administration. Sweating was observed in almost all ponies at both dose levels. The mean duration of analgesia was comparatively more (41.61 min.) in ponies given xylazine @ 1.1 mg/kg body weight than the those given @ 0.5 mg/kg body weight (32.66 min.). It appears that lower dose of 0.5 mg/kg body weight is

sufficient enough to induce satisfactory analgesia in ponies without much alteration in physiological indices.

Chitale *et al.* (1999) observed increased serum glucose level after administration of ketamine premedicated with α_2 agonists and diazepam in goats. Serum cholesterol and bilirubin levels were within physiological range.

Kinjavdekar *et al.* (1999) presented a comprehensive review of the different α-2 agonists including xylazine which are employed as agents for the production of spinal anaesthesia in different species of animals.

Pratap *et al.* (1999) reported that ketamine @ 3 mg/kg and ketamine @ 3 mg/kg along with xylazine @ 0.05 mg/kg were administered epidurally in 10 buffalo calves respectively in group A and group B. An early onset of analgesia was recorded in group B. The analgesia was good at perineum and moderate at tail in group B than group A. Sedation, motor incoordination were more pronounced and duration of analgesia was also more in group B. It was concluded that xylazine and ketamine combination produced good surgical analgesia of hind quarter in buffalo calves when used epidurally.

Singh *et al.* (1999) reported the biochemical alterations following induction of ketamine (@ 12 mg/kg body weight), ketamine+diazepam (@ 1mg/kg) and ketamine + lorazepam (@ 0.2 mg/kg) in 6 goats each of group I, II and III were studied. Atropine sulphate (@ 0.05 mg/kg) was administered to all the 18 goats half an hour before anaesthesia. Hyperglycaemia of varying magnitude was evidenced in all the groups but it had tendency to normalize by 24 hours. AST did not show significant alterations except in group III where significant rise in AST was seen. Change in BUN level fluctuated within physiological range.

Kinjavdekar (2001) observed an increase in serum glucose, creatinine and urea nitrogen when ketamine was used alone or in combination with xylazine or medetomidine. An increased in CVP and decrease in MAP was recorded when ketamine was used in combination with xylazine or medetomidine.

Phode and Aher (2003) reported a non-significant rise in blood urea nitrogen level at maximum depth of sedation and anaesthesia in bovine. They also observed a significant increase in blood glucose at the peak sedation and analgesia after administration of xylazine.

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CHAPTER - III

MATERIALS AND METHODS

MATERIALS AND METHODS

The present investigation was conducted on 15 clinically healthy non-descript she-goats aging one to two and half years and weighing in between 12 to 20 kg. The animals were maintained in the department of surgery and radiology under similar environmental conditions and uniform feeding schedules were adopted during pre and post anaesthetic periods. Green grasses and water were provided ad.lib. Daily grazing was allowed. The maintenance dose of concentrates were also supplied to them. Deworming was done 15 days prior to the experimentation and clinical examinations were conducted at a week interval during pre-experimental period to observed the state of health.

Design of the experiment :

The animals were randomly divided into 3 groups viz. I, II and III consisting of 5 animals in each group. The study included clinical, anaesthetic, and biochemical parameters.

In group I, Xylazine hydrochloride was administered i/m @ 0.4mg/kg b.wt. While in group II, Ketamine hydrochloride was administered i/m at the dose rate of 12 mg/kg b.wt. and in group III, a combination of xylazine-ketamine HCl was administered i/m at the dose rate of 0.4 mg and 12 mg/kg b.wt. respectively.

Anaesthetic Used :

***1. Xylazine Hydrochloride* :**

Indian Immunologicals.

****2. Ketamine HCl**** :**

Sterfil Laboratories Pvt. Ltd., Ankaleshwar

Methods of experimentation :

Preparation of the animals a day earlier to experimentation :

From the group of animals, one goat was selected randomly on which the experiment will be conducted the next morning. The region of the jugular vein was shaved. Food and water were withheld for 24 hours and 12 hours respectively before the start of the experiment.

Preparation of the animal just before the experiment :

The animal was weighed just before the administration of anaesthetics. Temperature, pulse and respiration rate of the experimental animals were recorded.. The site was washed with soap and water and painted with 70% alcohol before the administration of drug and drug combination. The values of the different parameters were noted and the blood samples were collected for determination of the base value (0 hour) of the different biochemical parameters.

The computed dose of the drugs were administered intramuscularly in each groups separately.

After the administration of the anaesthetic agents, the appearance of different clinical and anaesthetic effects were noted and blood samples were collected at 1 hr., 2 hrs., 3hrs. and finally at 24 hrs. for the estimation of different biochemical parameters. Clinical and anaesthetic parameters were recorded at the time interval of 5, 10, 15, 20, 30, 45, 60, 75, 90, 105 and 120 minutes after medication as detailed below :

1. Clinical Observations :

Rectal temperature, pulse, respiration rate, colour of mucous membrane were observed pre and post induction of anaesthesia at the time intervals as mentioned above.

The effect of anaesthetic regimen on salivation was keenly observed. Time of voiding, stool and urine were also recorded after induction of anaesthetic drugs.

2. Anaesthetic Observations :

Period of induction, duration of anaesthesia and recovery periods were recorded in all of the experimental animals.

The effects of analgesia on the status of different reflexes like corneal, palpebral, pedal and cutaneous were marked. The extent and magnitude of analgesia was ascertained by pin-prick response and was recorded using 0 - 3 scale.

0 – No analgesia – Strong reaction to pin-prick.

1 – Mild analgesia – Weak response to pin-prick.

2 – Moderate analgesia – Occasional response to pin-prick.

3 – Strong/Complete analgesia – No response to pin-prick.

Sedation was judged by recording drowsiness and lowering of head. The posture was recorded as :

0 – Alert

1 – Slight hind leg weakness

2 – Standing with great difficulty.

3 – Recumbent.

Effect of drug on the region of limbs, tail, perineum, udder, thigh, digit, posterior flank, anterior flank, thorax, ear and head were noted at different time intervals. Response to painful stimuli and pain threshold were assessed by pin-pricks, pinching the cutaneous and deeper structures by towel clamps or forceps. Period of induction, duration of anaesthesia and

recovery period as well as start of ambulation were noted on the basis of physical symptoms and reflexes.

3. Biochemical Parameters :

The following parameters were evaluated.

1. Serum glucose : Glucose-Oxidase (GOD) method
2. Serum urea : Diacetyl monoxime (DAM) method (Skeggs, 1957).
3. Serum creatinine : Alkaline picrate method.

For harvesting blood serum, 5 ml of blood was collected in each test tube without anticoagulant by dry syringe from the jugular vein. The blood was allowed to clot within the tube in a slanting position for 2 hours. Then, the serum was pipetted out carefully in another test tube and centrifused at 3,500 rpm for 10 minutes. The supernatant serum was collected with a rubber bulb pipette. Thereafter, the harvested serum was analysed for different biochemical parameters immediately.

(i) Glucose Estimation :

Serum glucose was estimated by Glucose-oxidase (GOD) Method. The principle behind it was that glucose was oxidized by glucose oxidase to gluconic acid and hydrogen peroxide. In subsequent peroxidase catalyzed reaction, the oxygen liberated was accepted by the chromogen system to give a red coloured quinoneamine compound. The red colour so developed was measured at 505 nm and was directly proportional to glucose concentration. All reagents (Clinical Chemistry Division of Span Diagnostics Ltd.) were brought to room temperature..

Reagents (Supplied in the kit) :

Reagent 1 : Glucose Enzyme Reagent.

Reagent 2 : Glucose Diluent

Reagent 3 : Glucose Standard, 100 mg%

Preparation of working glucose reagent :

4 x 50 ml pack : Quantitatively transferred the contents of one vial of Glucose Reagent (Reagent 1) to a black plastic bottle (provided in the kit) and reconstituted with 50 ml Glucose Diluent (Reagent-2). It was mixed slowly and dissolved completely.

Procedure (For Spectrophotometer) :

Reagent	Blank (B)	Standard (S)	Test (T)
Serum	-	-	0.02 ml
Glucose Standard, 100 mg/%	-	0.02 ml	-
Working Glucose Reagent	1.5 ml	1.5 ml	1.5 ml
Purified water	1.5 ml	1.5 ml	1.5 ml

All the test tubes were mixed well and the test tubes were kept in incubator and incubated at 37^0C for 10 minutes and their O.D. of standard (S) and Test (T) were measured at 505 nm against purified water with the help of colorimeter.

Calculation :-

$$\text{Serum Glucose in mg/100 ml} = \frac{\text{O.D. Test}}{\text{O.D. Standard}} \times 100$$

(iii) Quantitative Determination of Urea in serum :

Urea concentration in serum was estimated by Diacetyl Monoxime (DAM) Method (Skeggs, 1957) in order to investigate the kidney function before and after the administration of drug and drug combination. The procedure followed is briefly described here under.

Intended use :

Reagents supplied in the kit.

Principle :

In acidic medium, serum urea reacted with hot diacetyle monoxime to produce rose - purple coloured complex, the intensity of which was proportional to the concentration of urea in sample and it was measured colorimetrically at 525 nm.

Reagent preparation :

R-1 : Diluted 1.0 ml of Urea reagent to 5 ml with distilled water.

Kit supplied R-2 and 3 were ready for use.

Procedure :

Reagent	Blank (B)	Standard (S)	Test T
Working Reagent (R_1)	5.0 ml	5.0 ml	5.0 ml
Serum	-	-	0.02 ml
Standard	-	0.020 ml	-
DAM Reagent	0.5 ml	0.5 ml	0.5 ml

All the tubes were mixed well and kept the tubes for exactly 10 minutes in boiling water bath. A rose - purple colour appeared as a result of reaction of urea with diacetyl monoxime in acidic medium. The test tubes

were cooled in running tap water for 5 minutes and O.D. of all the tubes were measured at 525 nm against blank adjusted to zero.

Calculation :

$$\text{Serum Urea Concentration in mg \%} = \frac{\text{O.D. of test}}{\text{O.D. of standard}} \times 30$$

(iii) Quantitative estimation of creatinine in the serum :

In-vitro, the estimation of creatinine was done by Alkaline picrate method. The principle lies behind it was that creatinine in a protein free solution reacted with alkaline picrate and produced an orange coloured complex. The estimation was done with reagents supplied in the kit.

Reagent Preparation :

Working Standard : Diluted 0.1 ml of reagent 3 (creatinine standard) with 10 ml of distilled water.

Reagent 1 and 2 were ready for use.

Procedure :

The estimation involved two steps :

Step A : Deproteinization of test sample

Serum	:	1.0 ml
Distilled water	:	1.0 ml
Reagent 1 : Picric acid	:	6.0 ml

All the tubes were mixed well and kept in a boiling water bath for 60 seconds then cooled under running tap water and the precipitated product was filtered through Whatman no. 1 filter paper.

Step B : Colour development :

	B	T	S
Filtrate (from step A)	-	4.0 ml	-
Working standard	-	-	1.0 ml
Distilled water	1.0 ml	-	-
Reagent 1 : Picric acid	3.0 ml	-	3.0 ml
Reagent 2 :			
Sodium Hydroxide, 0.75 N	1.0 ml	1.0ml	1.0ml

All the tubes were mixed well and allowed to stand at R.T. for 20 minutes and immediately O.D. of blank, standard and test were measured against distilled water, at 520 nm.

Calculations :

$$\text{Serum creatinine O.D. test} - \text{O.D. blank in mg \%} = \frac{\text{O.D. test-O.D. blank}}{\text{O.D. std-O.D. blank}} \times 3.0$$

Statistical Analysis :

Data were analysed by standard statistical methods as described by Snedecor and Cochran (1967).

The variations in different traits due to period and group were estimated by F test and mean differences were tested by critical difference test as described by Snedecor and Cochran (1967).

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CHAPTER - IV

OBSERVATION AND RESULT

OBSERVATION AND RESULT

Clinical Parameter

Rectal Temperature :

Mean along with their S.E. of rectal temperature in anesthetized goats at different period of interval have been presented in table- 1. The rectal temperature did not vary significantly at different period of interval after induction with xylazine hydrochloride, ketamine hydrochloride and the combination of xylazine and ketamine hydrochloride in three different groups of goats. However, in all three groups the rectal temperature was marked declined slightly but increased nearer to the level of base value 0 (Zero) minute at 120^{th} minute of experiment in general. The analysis of variance (Table - 1A) did not reveal significant difference in rectal temperature between periods in each group. The minimum temperature was 100.28 ± 0.73^0 F at 45 minutes in group I, 101.92 ± 0.15^0 F at 90 minutes in group II and 100.74 ± 0.31 ^{0}F at 45 minutes in group III (Table - 1).

Table – 1 revealed that the effect of anaesthetic agents did not have any significant effect on rectal temperature in group I, II, and III. The analysis of variance did not reveal any significant effect of anaesthetic agents on rectal temperature in goats up to 120^{th} minute of experiment (Table – 1B).

Pulse rate :

Mean along with their S.E. of Pulse rate in anaesthetized goats at different period of interval have been presented in table – 2. The average

Table : 1. Mean ± S.E. of rectal temperature of anaesthetic goats at different periods of interval.

Group	Period (minutes)											
	0	5	10	15	20	30	45	60	75	90	105	120
I	101.76 ± 0.28	101.26 ± 0.45	101.08 ± 0.48	101.08 ± 0.48	100.96 ± 0.54	100.28 ± 0.73	100.28 ± 0.73	100.38 ± 1.07	100.66 ± 1.20	101.16 ± 1.02	101.24 ± 0.99	101.86 ± 0.69
II	102.02 ± 0.16	102.08 ± 0.17	102.10 ± 0.17	102.14 ± 0.19	102.02 ± 0.18	101.96 ± 0.19	102.14 ± 0.24	102.14 ± 0.24	101.98 ± 0.21	101.92 ± 0.15	101.92 ± 0.15	101.92 ± 0.15
III	101.34 ± 0.37	101.34 ± 0.37	101.34 ± 0.37	101.50 ± 0.22	101.38 ± 0.29	101.14 ± 0.33	100.74 ± 0.31	100.84 ± 0.43	101.10 ± 0.62	101.56 ± 0.58	101.86 ± 0.68	101.86 ± 0.68

Table – 1A

Analysis of variance for the effect of anaesthetic agents on rectal temperature in goats.

Group	Source of Variation	df.	M.S.	F.
Group I	Between periods	11	4.92	1.64^{NS}
	Error	48	2.98	
Group II	Between periods	11	0.03	0.17^{NS}
	Error	48	0.18	
Group III	Between periods	11	1.91	1.75^{NS}
	Error	48	1.08	

NS = (Non-significant)

Table – 1B

Analysis of variance for the effect of anaesthetic agents on rectal temperature in goats at different periods of interval.

Period	Source of variation	df	M.S.	F
0 Min.	Between group	2	0.59	1.46^{NS}
	Error	12	0.40	
5 Min.	Between group	2	1.02	1.89^{NS}
	Error	12	0.53	
10 Min.	Between group	2	1.41	2.08^{NS}
	Error	12	0.67	
15 Min.	Between group	2	1.43	2.67^{NS}
	Error	12	0.53	
20 Min.	Between group	2	1.42	2.08^{NS}
	Error	12	0.68	
30 Min.	Between group	2	3.52	3.11^{NS}
	Error	12	1.13	
45 Min.	Between group	2	3.69	2.97^{NS}
	Error	12	1.24	
60 Min.	Between group	2	8.21	3.12^{NS}
	Error	12	2.63	
75 Min.	Between group	2	13.08	3.15^{NS}
	Error	12	4.14	
90 Min.	Between group	2	7.90	3.00^{NS}
	Error	12	2.53	
105 Min.	Between group	2	8.62	2.49^{NS}
	Error	12	3.46	
120 Min.	Between group	2	6.74	2.56^{NS}
	Error	12	2.63	

estimates of pulse rate did not observe to be varied significantly between group I and II upto 15 minutes after the induction of anaesthetic agents whereas in group III the pulse rate was observed increased significantly ($P<0.01$) than group I and II by 3 and 4.2 per minute at 10^{th} minute. 8.8 and 5.2 at 15 minutes and 9.2 and 4.4 at 20^{th} minute respectively. The analysis of variance revealed significant difference in pulse rate between the groups from 10 minute onwards following the administration of the drugs (Table – 2B). From 20 minutes onwards upto 120^{th} minute, the pulse rate of anaesthetized goats in group I was observed to be significantly ($P<0.01$) lowered than the pulse rate of anaesthetized goats in group II and III in general, however, at 120^{th} minute the difference was non significant between group I and III. After 30 minutes following administration of the drugs the difference in pulse rate between group II and III was non significant, however, from 45^{th} to 105^{th} minute the average estimated pulse rate in group II was significantly ($P<0.01$) increased than the pulse rate in group III and the difference was non significant at 120^{th} minute.

The analysis of variance revealed significant difference among average pulse rate in each group at different periods of interval (Table – 2A). Prior to the administration of drugs i.e. at 0 (Zero) minute, the average pulse rate in group I, II and III were recorded 74.0 ± 0.78, 73.40 ± 0.87 and 74.80 ± 1.02 per minute respectively. The average pulse rate in group I was observed significantly ($P<0.01$) decreased gradually from 15 minutes onwards, however, at 120^{th} minute the pulse rate was lowered but differences were non significant.

Table : 2. Mean ± S.E. of Pulse rate of anaesthetic goats at different periods of interval.

	Period (minutes)											
Group	0	5	10	15	20	30	45	60	75	90	105	120
I	74.00^{Ad} ± 0.78	74.00^{Ad} ± 0.78	74.00^{Bd} ± 0.78	70.00^{Be} ± 1.00	69.00^{Ce} ± 0.70	69.00^{Be} ± 0.78	67.40^{Cef} ± 0.87	66.80^{Cf} ± 0.73	65.00^{Cf} ± 0.84	66.40^{Cf} ± 0.51	68.60^{Cefg} ± 0.40	72.60^{Bdg} ± 0.40
II	73.40^{Ad} ± 0.87	73.40^{Ad} ± 0.87	73.40^{Bd} ± 0.87	73.60^{Bd} ± 0.81	74.80^{Bd} ± 0.86	79.00^{Aef} ± 1.92	82.80^{Ae} ± 1.53	82.00^{Ae} ± 1.24	81.60^{Ae} ± 1.03	78.00^{Af} ± 0.78	76.40^{Afg} ± 0.81	74.40^{Adf} ± 0.81
III	74.80^{Ad} ± 1.02	75.60^{Ad} ± 1.08	77.60^{Ae} ± 1.08	78.80^{Ae} ± 1.08	78.20^{Ae} ± 2.18	77.60^{Ae} ± 1.25	75.60^{Bd} ± 1.25	74.40^{Bd} ± 1.54	73.40^{Bd} ± 1.28	73.80^{Bd} ± 1.05	73.60^{Bd} ± 1.07	73.40^{ABd} ± 0.93

A – C; Values bearing same superscript in a column did not differ significantly.

d – h; Values bearing same superscript in a row did not differ significantly.

Table - 2 A

Analysis of variance for the effect of anaesthetic agents on pulse rate in goats.

Group	Source of Variation	df.	M.S.	F.
Group I	Between periods	11	71.37	28.17**
	Error	48	2.53	
Group II	Between periods	11	65.28	11.08**
	Error	48	5.89	
Group III	Between periods	11	50.85	5.78**
	Error	48	8.78	

** = Singnificant at ($p < 0.01$)

Table – 2B

Analysis of variance for the effect of anaesthetic agents on pulse rate in goats.

Period	Source of variation	df	M.S.	F
0 Min.	Between group	2	16.46	1.86^{NS}
	Error	12	8.84	
5 Min.	Between group	2	26.01	2.69^{NS}
	Error	12	9.67	
10 Min.	Between group	2	79.8	19.78**
	Error	12	4.03	
15 Min.	Between group	2	122.86	16.75**
	Error	12	7.33	
20 Min.	Between group	2	157.86	15.84**
	Error	12	9.96	
30 Min.	Between group	2	136.26	14.19**
	Error	12	9.60	
45 Min.	Between group	2	265.86	34.23
	Error	12	7.76	
60 Min.	Between group	2	320.60	43.32**
	Error	12	7.40	
75 Min.	Between group	2	344.46	60.43**
	Error	12	5.7	
90 Min.	Between group	2	236.60	76.32**
	Error	12	3.10	
105 Min.	Between group	2	210.2	64.36**
	Error	12	3.26	
120 Min.	Between group	2	208.06	74.30**
	Error	12	2.80	

NS = Non-significant

**** = Significant ($p<0.01$)**

In group II, the average pulse rates were observed significantly ($p<0.01$) increased from 30th minute onwards upto 105th minute and it was maximum at 60th minute. From 75th minute onwards, the pulse rates were observed decreased gradually, however, the difference between base value at 0 (zero) minute and at 120th minute was non-significant.

In group III, the average pulse rates were observed significantly ($P<0.01$) increased from 10th to 30th minute and it was maximum at 15th minute. From 45th minute onwards the average pulse rates were observed significantly lower than the pulse rate at 30th minute, however, the differences were non significant from the base value at 0 (Zero) minute.

Respiration rate :

Mean along with their S.E. of respiration rate of anaesthetized goats at different periods of interval have been presented in table – 3. There was no significant difference in between group II and III from 5th to 20th minute after the induction of anaesthetic agents, whereas in group I the respiration rate observed to be decreased significantly ($P<0.01$) than group II and III.

The analysis of variance (Table – 3B) revealed significant difference in respiration rate between the groups from 5 minutes onwards following the administration of the drugs. From 30 minutes onwards upto 90th minute the respiration rate of anaesthetized goats in group I was marked to be significantly ($P<0.01$) lower than the respiration rate of anaesthetized goats in group II and III in general, however, from 105th to 120th minute, the respiration rate showed tendency to return to its base values 0 (Zero) minute in group I and III.

Table : 3. Mean ± S.E. of respiration rate of anaesthetic goats at different periods of interval.

	Period (minutes)											
Group	0	5	10	15	20	30	45	60	75	90	105	120
I	21.00^{Ad} ± 0.44	17.40^{Cg} ± 0.51	17.40^{Cg} ± 0.51	17.40^{BCg} ± 0.51	17.40^{BCg} ± 0.51	17.80^{Cfg} ± 0.49	18.40^{Cefg} ± 0.68	19.40^{Cdef} ± 0.51	19.40^{Cdef} ± 0.51	19.40^{Cdef} ± 0.51	20.00^{Bde} ± 0.63	20.20^{Bd} ± 0.49
II	19.80^{Af} ± 0.97	19.80^{ABf} ± 0.97	19.80^{ABf} ± 0.97	19.80^{Bf} ± 0.97	20.60^{ABef} ± 1.69	20.60^{Bef} ± 1.69	24.20^{ABd} ± 0.73	24.40^{Ad} ± 0.68	24.00^{Ad} ± 0.32	24.00^{Ad} ± 0.37	23.00^{Ade} ± 0.45	23.00^{Ade} ± 0.45
III	21.00^{Af} ± 0.32	21.40^{Af} ± 0.67	21.60^{Aef} ± 0.51	22.20^{Aef} ± 0.58	22.60^{Ade} ± 0.24	23.60^{Ad} ± 0.24	23.40^{Ad} ± 0.24	23.20^{ABde} ± 0.20	23.00^{ABde} ± 0.31	22.60^{Bde} ± 0.24	20.60^{Bf} ± 0.24	20.80^{Bf} ± 0.21

A – C; Values bearing same superscript in a column did not differ significantly.

d – h; Values bearing same superscript in a row did not differ significantly.

Table – 3 A

Analysis of variance for the effect of anaesthetic agents on respiration rate in goats.

Group	Source of Variation	df.	M.S.	F.
Group I	Between periods	11	11.35	6.98**
	Error	48	1.62	
Group II	Between periods	11	19.90	4.31**
	Error	48	4.61	
Group III	Between periods	11	5.59	8.22**
	Error	48	0.68	

** = Significant at ($p < 0.01$)

Table – 3 B

Analysis of variance for the effect of anaesthetic agents on respiration rate in goats.

Period	Source of variation	df	M.S.	F
0 Min.	Between group	2	2.40	1.16^{NS}
	Error	12	2.06	
5 Min.	Between group	2	20.27	7.34**
	Error	12	2.76	
10 Min.	Between group	2	22.20	9.13**
	Error	12	2.43	
15 Min.	Between group	2	28.80	11.25**
	Error	12	2.56	
20 Min.	Between group	2	34.40	6.49**
	Error	12	5.30	
30 Min.	Between group	2	42.07	7.99**
	Error	12	5.26	
45 Min.	Between group	2	49.40	28.06**
	Error	12	1.76	
60 Min.	Between group	2	34.07	27.03**
	Error	12	1.26	
75 Min.	Between group	2	29.27	38.51**
	Error	12	0.76	
90 Min.	Between group	2	27.80	39.71**
	Error	12	0.70	
105 Min.	Between group	2	12.60	11.45**
	Error	12	1.10	
120 Min.	Between group	2	10.87	13.58**
	Error	12	0.80	

NS = Non-significant

**** = Significant at ($p<0.01$)**

The analysis of variance (Table – 3A) revealed significant difference among average respiration rates in each group of different periods of interval. Prior to the administration of drugs i.e. at 0 (Zero) minute, the average respiration rates in group I, II and III were observed 21.00 ±0.44, 19.80±0.97 and 21.00 ±0.32 per minute respectively. The average respiration rate in group I was observed to be decreased significantly ($P<0.01$) following administration of the drug upto 45th minute. Then, there was gradual increase which was marked nearer to base value at 120th minute of experiment.

In group II, the average respiration rates were observed significantly ($P<0.01$) increased from 45th minute onwards following the administration of the drugs upto 120th minutes and it was maximum at 60 minutes and then slightly decreased upto 120th minute from the base value at 0 (zero) minute.

In group III, the average respiration rates were observed significantly ($P<0.01$) increased from 20th to 75th minute and then from 90 minutes onwards it gradually decreased upto 120th minute. From 45 minutes onwards the respiration rates were observed significantly ($P<0.01$) lower than the respiration rates at 30 minutes, however, the differences were non significant from the base value at 0 (zero) minute.

Anaesthetic parameters :

Onset of action :

Time from injection of anaesthetic agents to loss of sensation (recumbency) was considered as onset of action.

Mean along with their S.E. of onset of action (in minutes) in anaesthetized goats in different experimental groups of goats have been presented in table – 4. The average estimates of onset of action (in minutes) were observed 3.24 ± 0.03, 5.85 ± 0.35 and 2.67 ± 0.19 in group I, II and III respectively. The onset of action was significantly ($p<0.01$) quicker in group III than group I and II, however, group I was also significantly ($p<0.01$) quicker than group II. Analysis of variance (Table – 4A) revealed that there was significant ($p < 0.01$) difference in between group I, II and III after the induction of anaesthetic agents.

Duration of action :

Time from the onset of action to return of sensation on entire body of the experimental animal was considered as duration of action.

Mean along with their S.E. for duration of action (in minutes) in anaesthetized goats in different experimental groups have been presented in table – 4. The average estimates for duration of action (in minutes) were observed 68.00 ± 3.39, 38.00 ± 1.22 and 85.00 ± 1.58 in group I, II and III respectively. The duration of action was significantly ($p<0.01$) longer in group III than group I and II, however, group I was also significantly ($p<0.01$) longer than group II. Analysis of variance (Table – 4A) revealed significant ($p<0.01$) difference in between group I, II and III after the induction of anaesthetic agents.

Recovery period :

Time from injection of anaesthetic agents until animal could stand and walk voluntarily was considered as recovery period.

Table – 4 : Mean ± S.E. of onset of action, duration of action and recovery period of anaesthetic agents in different experimental groups of goats.

Group	Onset of action (in minutes)	Duration of action (in minutes)	Recovery period (in minutes)
I	$3.24^{b} \pm 0.03$	$68.00^{b} \pm 3.39$	$89.00^{b} \pm 1.87$
II	$5.85^{a} \pm 0.35$	$38.00^{c} \pm 1.22$	$43.00^{c} \pm 1.22$
III	$2.67^{c} \pm 0.19$	$85.00^{a} \pm 1.58$	$110.00^{a} \pm 2.24$

Value bearing same superscript did not differ significantly.

Table – 4A : Analysis of variance for the effect of different anaesthetic agents on the onset of action, duration of action and recovery period at different time intervals.

Parameters	Source of variation	d.f.	m.s.	F
Onset of action	Between groups	2	15.98	59.74**
	Within group	12	0.27	
Duration of action	Between groups	2	2986.67	115.62**
	Within group	12	25.83	
Recovery period	Between groups	2	5161.67	309.83**
	Within group	12	16.66	

** = Significant at ($p<0.01$)

Mean along with their S.E. of recovery period (in minutes) in anaesthetized goats in different experimental groups have been presented in table – 4. The average estimates of recovery period (in minutes) were observed 89.00 ± 1.87, 43.00 ± 1.22 and 110.00 ± 2.24 in group I, II and III respectively. The recovery period was significantly ($p<0.01$) longer in group III than group I and II, however, group I was also significantly ($p<0.01$) longer than group II. Analysis of variance (Table – 4A) revealed that there was significant ($p<0.01$) difference in between group I, II and III after the induction of anaesthetic agents.

Analgesia :

Mean along with their S.E. of scale of analgesia in anaesthetized goats in different experimental groups have been presented in table-5. Analgesia was recorded using a 0 - 3 scale to pin-prick response in entire region of the anaesthetized goat. In group I, analgesia was started from 5 minutes of injection and continued upto 120 minutes. On 0 - 3 scale, the range of analgesia was variable and observed from 0 to 2. From 20 to 45 minutes, moderate analgesia was observed and from 5 to 15 minutes and from 60 to120 minutes, mild analgesia was recorded. The maximum analgesia mean value of the scale of analgesia was 2.00 ± 0.00 whereas its individual value ranged between 1 to 2 till 15 to 75 minutes of observation.

In group II, there was also mild to moderate analgesia but moderate analgesia was for very short duration about 10 minutes only. Analgesia started from 10 minutes and lasted for 60 minutes. The maximum analgesia mean value was 2.00 ± 0.00.

Table - 5

Showing mean ± S.E. of scale of analgesia after administration of xylazine, ketamine and their combination.

	Time Interval (minutes)											
Drug	0	5	10	15	20	30	45	60	75	90	105	120
Xylazine	0.00 ± 0.00	0.65 ± 0.01	0.65 ± 0.01	1.54 ± 0.04	2.00 ± 0.00	2.00 ± 0.00	2.00 ± 0.00	1.48 ± 0.01	1.48 ± 0.01	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00
Ketamine	0.00 ± 0.00	0.00 ± 0.00	0.50 ± 0.03	1.35 ± 0.03	2.00 ± 0.00	2.00 ± 0.00	1.35 ± 0.01	0.53 ± 0.01	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
Xylazine + Ketamine	0.00 ± 0.00	2.00 ± 0.00	2.37 ± 0.01	3.00 ± 0.00	3.00 ± 0.00	3.00 ± 0.00	3.00 ± 0.00	2.34 ± 0.08	2.20 ± 0.02	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00

In group III, moderate to excellent analgesia was observed with longer duration of action. Analgesia started within 5 minutes and continued upto 120 minutes. On 0 -3 analgesic scale, peak mean value was 3.00 ± 0.00 from 15 to 45 minutes as all the animals exhibited uniform scale 3 level analgesia on the individual basis during this period. It means all the animals after receiving xylazine-ketamine combination manifested the level of analgesia which was perfect scale 3 level analgesia. In other time intervals analgesic scale ranged from 0 -3. This combination was best among the other two groups owing to its longer duration of action and strongest analgesic properties.

Sedation :

Mean along their S.E. of scale of sedation in anaesthetized goats in different experimental groups have been presented in table-6. In group I, mild to moderate sedation was observed which started after 5 minutes of injection and lasted for 60 minutes. The maximum mean value of sedation was 2.55 ± 0.00 and individual range of sedation was 1 to 3 on 0 -3 sedation scale. In group II, there was mild sedation with longer duration which started from 5 minutes and lasted upto 60 minutes. The maximum mean value of sedation and its individual value 1.60 ± 0.00 and 1 to 2 at 10 to 45 minutes time of interval was recorded on 0 -3 scale. In group III, moderate to excellent sedation was observed after administration of the xylazine-ketamine combination. The sedation was evident after 5 minutes of induction and continued upto 90 minutes. The maximum mean value and its individual ranged on the 0 -3 scale of sedation as 3.00 ± 0.00 and 3 to 3

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Table - 6

Showing mean ± S.E. of scale of sedation after administration of xylazine, ketamine and their combination.

	Time Interval (minutes)											
Drug	0	5	10	15	20	30	45	60	75	90	105	120
Xylazine	0.00 ± 0.00	1.91 ± 0.04	1.91 ± 0.04	2.55 ± 0.00	2.55 ± 0.00	2.39 ± 0.02	1.68 ± 0.02	1.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
Ketamine	0.00 ± 0.00	0.67 ± 0.02	1.07 ± 0.18	1.60 ± 0.00	1.60 ± 0.00	1.60 ± 0.00	1.38 ± 0.01	0.55 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
Xylazine + Ketamine	0.00 ± 0.00	2.55 ± 0.01	2.55 ± 0.01	3.00 ± 0.00	3.00 ± 0.00	3.00 ± 0.00	3.00 ± 0.00	3.00 ± 0.00	2.62 ± 0.03	2.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00

respectively at 15 to 60 minutes. But in all other period of observations individual scale of sedation ranged between 2 to 3. This combination was best among all groups due to long duration and strong sedative properties.

Reflexes :

Different reflexes after administration of xylazine, ketamine and their combination in goats have been presented in table 7, 7A and 7B. In group I, corneal reflex was light at 15 to 20 and at 60 minutes, absent at 30 to 45 minutes and rest of the time interval normal reflexes were observed. Palpebral reflex was sluggish at 15 to 20 and 60 minutes and at 30 to 45 minutes reflexes were absent. Thereafter, palpebral reflexes were observed normal. Cutaneous reflex was absent from 5 to 60 minutes and sluggish at 75 minutes. Then, it was present till 120 minutes. Pedal reflex was observed light at 5 to 10 minutes after which it became completely absent from 15 to 60 minutes. Thereafter, it remained sluggish till 75 minutes and present till 120 minutes of experiment.

In group II, corneal and palpebral reflexes were present throughout the observation periods except at 20 minutes where as corneal reflex was light and palpebral reflex was sluggish. Cutaneous and pedal reflexes were absent at 15 to 30 minutes. Thereafter, it became normal throughout the observation periods. In group III, corneal and palpebral reflexes were normal throughout the observation period. These reflexes, even though present, were greatly depressed in all the animals. Cutaneous reflex was completely absent from 5 to 75 minutes and then it became sluggish upto 120 minutes.

Table - 7

Showing the status of different reflexes after administration of xylazine.

Time interval (minutes)	Corneal reflex	Palpebral reflex	Cutaneous reflex (Ant. and Post flank)	Pedal reflex
0	Present	Present	Present	Present
5	Present	Present	Absent	Light
10	Present	Present	Absent	Light
15	Light	Sluggish	Absent	Absent
20	Light	Sluggish	Absent	Absent
30	Absent	Absent	Absent	Absent
45	Absent	Absent	Absent	Absent
60	Light	Sluggish	Absent	Absent
75	Present	Present	Sluggish	Sluggish
90	Present	Present	Present	Present
105	Present	Present	Present	Present
120	Present	Present	Present	Present

Table - 7A

Showing the status of different reflexes after administration of ketamine.

Time interval (minutes)	Corneal reflex	Palpebral reflex	Cutaneous reflex (Ant. and Post flank)	Pedal reflex
0	Present	Present	Present	Present
5	Present	Present	Present	Present
10	Present	Present	Present	Present
15	Present	Present	Absent	Absent
20	Light	Sluggish	Absent	Absent
30	Present	Present	Absent	Absent
45	Present	Present	Present	Present
60	Present	Present	Present	Present
75	Present	Present	Present	Present
90	Present	Present	Present	Present
105	Present	Present	Present	Present
120	Present	Present	Present	Present

Table - 7B

Showing the status of different reflexes after administration of xylazine - ketamine combination.

Time interval (minutes)	Corneal reflex	Palpebral reflex	Cutaneous reflex (Ant. and Post flank)	Pedal reflex
0	Present	Present	Present	Present
5	Present	Present	Absent	Absent
10	Present	Present	Absent	Absent
15	Present	Present	Absent	Absent
20	Present	Present	Absent	Absent
30	Present	Present	Absent	Absent
45	Present	Present	Absent	Absent
60	Present	Present	Absent	Absent
75	Present	Present	Absent	Absent
90	Present	Present	Sluggish	Light
105	Present	Present	Sluggish	Light
120	Present	Present	Sluggish	Light

Pedal reflex was found absent from 5 minutes to 75 minutes and then it became light upto 120 minutes.

Biochemical Parameter :

Blood glucose :

Mean along with their standard errors for blood glucose at different period of interval under the influence of different anaesthetic agents in goats have been presented in Table – 8. The average level of blood glucose were observed 49.53 ±1.28, 53.00 ± 2.26 and 50.15 ± 1.56 in group I, II and III respectively. The analysis of variance did not reveal significant difference between groups in general except at 1st hour after the induction of anaesthetic agents (Table-8A). The mean blood glucose level was significantly higher in group III as compared to group I and II by 27.37 and 27.05 mg / 100 ml respectively. However, no significant difference could be detected in group I and II at 1st hour after the induction of anaesthetic agent.

The average estimates of blood glucose level in all three groups were observed to be increased significantly upto 3 hours than the base value at 0 (Zero) hour. The analysis of variance (Table-8B) revealed significant ($P<0.01$) difference in blood glucose level in all three groups. The mean blood glucose level in group I was significantly ($P<0.01$) increased by 14.14 mg/100 ml at 1st hour after the induction of the anaesthetic agent. The level was 10.99 mg/100ml and 40.89 mg/100 ml in group II and III respectively at the same period of time. the average estimates of blood glucose level in all the three groups at 24th hour after induction of the agents were very closer to the base value at 0 (Zero) hour and did not differ significantly.

Table – 8.

Mean ± S.E. of blood glucose (mg/100ml) of goats at different periods of interval under the influence of anaesthetic agents.

Period (Hours)

Group	Dose	0	1	2	3	24
I	0.4 mg/kg	$49.53^{z} \pm 1.28$	$63.67^{by} \pm 3.19$	$76.39^{x} \pm 2.20$	$74.09^{x} \pm 2.27$	$49.13^{z} \pm 0.92$
II	12 mg/kg	$53.00^{z} \pm 2.26$	$63.99^{by} \pm 1.15$	$76.39^{x} \pm 4.00$	$82.64^{x} \pm 4.04$	$53.18^{z} \pm 2.71$
III	0.4 mg/kg + 12 mg/kg	$50.15^{z} \pm 1.56$	$91.04^{ax} \pm 2.77$	$86.60^{xy} \pm 2.90$	$81.44^{y} \pm 4.08$	$48.48^{z} \pm 1.24$

a-b : Values bearing same superscript in a column did not differ significantly.

x-z : Values bearing same superscript in a row did not differ significantly.

Table - 8A

Analysis of variance for the effect of anaesthetic agents on blood glucose (mg/100ml) in goats.

Period	Source of Variation	df.	M.S.	F.
0 Hr.	Between groups	2	17.11	1.12^{NS}
	Error	12	15.23	
1 Hr.	Between groups	2	1233.65	38.57**
	Error	12	31.97	
2 Hrs.	Between groups	2	173.74	3.56^{NS}
	Error	12	48.77	
3 Hrs.	Between groups	2	106.99	1.68^{NS}
	Error	12	63.55	
24 Hrs.	Between groups	2	32.48	2.00^{NS}
	Error	12	16.21	

Table - 8B

Analysis of variance for the effect of anaesthetic agents on blood glucose (mg/100ml) in goats.

Group	Source of Variation	df.	M.S.	F.
Group I	Between periods	4	844.46	37.32**
	Error	20	22.62	
Group II	Between periods	4	902.71	19.56**
	Error	20	46.15	
Group III	Between periods	4	2117.97	57.73**
	Error	20	36.68	

** = Significant at ($p<0.01$)

Blood urea nitrogen :

Mean along with their S.E. of blood urea nitrogen at different periods of interval under the influence of different anaesthetic agents in goats have been presented in table – 9. The average estimate of blood urea nitrogen at 0 (Zero) hour was observed 23.34 ± 0.54, 23.85 ± 0.34 and 23.67 ± 0.66 mg % in group I , II and III respectively. The analysis of variance(Table – 9A) did not reveal any significant difference in between groups at different periods of interval following the induction of anaesthetic agents.

The average estimates of blood urea nitrogen level were observed with non significant difference in all the three groups. The analysis of variance (Table-9B) revealed significant difference between mean value of blood urea nitrogen at different periods of interval in group I ($P<0.01$) and II ($P<0.05$). The mean blood urea nitrogen level in group I was observed significantly ($P<0.01$) increased by 2.82 and 1.96 mg% at 1st and 2nd hour after the induction of anaesthetic agents from the base value at 0 (Zero) hour. In group II, a significant ($P<0.05$) increase in blood urea nitrogen level was observed at 2nd hour after the induction of anaesthetic agent by 1.85 mg%. Then, the mean values were marked declining from 3rd hour onwards. However, it came to normal at 24th hour post medication.

In group III, an increase in the mean blood urea nitrogen level was observed at 1st and 2nd hour following the induction of anaesthetic agents but non significant difference could be detected among the different groups.

Table – 9.

Mean ± S.E. of blood urea nitrogen (BUN) (mg%) of goats at different periods of interval under the influence of anaesthetic agents.

Period (Hours)

Parameters	Dose	0	1	2	3	24
I	0.4 mg/kg	$23.34^{z} \pm 0.54$	$26.16^{x} \pm 0.38$	$25.30^{xy} \pm 0.42$	$24.27^{yz} \pm 0.41$	$23.48^{z} \pm 0.49$
II	12 mg/kg	$23.85^{yz} \pm 0.34$	$24.62^{xy} \pm 0.38$	$25.39^{x} \pm 0.22$	$24.16^{xyz} \pm 0.47$	$23.12^{z} \pm 0.67$
III	0.4 mg/kg + 12 mg/kg	23.67 ± 0.66	25.51 ± 0.42	24.24 ± 0.56	23.4 ± 0.81	22.93 ± 0.66

Values bearing same superscript in a row did not differ significantly.

Table - 9A

Analysis of variance for the effect of anaesthetic agents on blood urea nitrogen (BUN) (mg%) in goats.

Period	Source of Variation	df.	M.S.	F.
0 Hr.	Between groups	2	0.33	0.23^{NS}
	Error	12	1.41	
1 Hr.	Between groups	2	2.98	3.82^{NS}
	Error	12	0.78	
2 Hrs.	Between groups	2	2.54	2.83^{NS}
	Error	12	0.89	
3 Hrs.	Between groups	2	797.32	3.49^{NS}
	Error	12	228.39	
24 Hrs.	Between groups	2	0.39	0.20^{NS}
	Error	12	1.86	

Table - 9B

Analysis of variance for the effect of anaesthetic agents on blood urea nitrogen (BUN) (mg%) in goats.

Group	Source of Variation	df.	M.S.	F.
Group I	Between periods	4	7.29	7.12**
	Error	20	1.02	
Group II	Between periods	4	3.62	3.73*
	Error	20	0.97	
Group III	Between periods	4	4.87	2.39^{NS}
	Error	20	2.03	

NS = Non-significant

*** = Significant at ($p<0.05$)**

**** = Significant at ($p<0.01$)**

Creatinine :

Mean along with their S.E. of creatinine at different periods of interval under the influence of different anaesthetic agents in goats have been presented in table – 10. The average estimates of cretinine at 0 (Zero) hour were found 1.31 ± 0.03, 1.35 ± 0.07 and 1.50 ± 0.05 mg% in group I, II and III respectively. The analysis of variance (Table 9A) revealed significant ($P<0.01$) difference in between group at 1, 2 and 3 hours respectively, while non significant difference was observed among different groups at 24 hrs following the induction of anaesthetic agents.

A significant increase ($p<0.01$) in the average level of creatinine was observed upto 3 hrs than the base value of the respective groups at 0 (Zero) hour. The analysis of variance (Table-10B) revealed non significant difference in group I and significant ($P<0.05$)
difference in group II and highly significant ($P<0.01$) difference in group III.

The average estimates of creatinine level in all three groups at 24^{th} hour after induction of agents were nearer to the mean base value at 0 (Zero) hour and did not differ significantly.

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Table - 10A

Analysis of variance for the effect of anaesthetic agents on creatinine (mg%) in goats.

Period	Source of Variation	df.	M.S.	F.
0 Hr.	Between groups	2	0.04	3.30^{NS}
	Error	12	0.01	
1 Hr.	Between groups	2	0.17	17.5**
	Error	12	0.01	
2 Hrs.	Between groups	2	0.32	29.54**
	Error	12	0.01	
3 Hrs.	Between groups	2	0.34	28.66**
	Error	12	0.01	
24 Hrs.	Between groups	2	0.04	3.75^{NS}
	Error	12	0.01	

** = Significant at ($p<0.01$)

Table – 10.

Mean ± S.E. of Creatinine (mg%) of goats at different periods of interval under the influence of anaesthetic agents.

Period (Hours)

Parameters	Dose	0	1	2	3	24
I	0.4 mg/kg	1.31 ± 0.03	$1.42^{b} \pm 0.04$	$1.39^{b} \pm 0.03$	$1.35^{b} \pm 0.04$	1.30 ± 0.03
II	12 mg/kg	$1.35^{xy} \pm 0.07$	$1.43^{bx} \pm 0.06$	$1.43^{bx} \pm 0.05$	$1.40^{bx} \pm 0.06$	$1.19^{y} \pm 0.06$
III	0.4 mg/kg + 12 mg/kg	$1.50^{y} \pm 0.05$	$1.75^{ax} \pm 0.04$	$1.85^{ax} \pm 0.06$	$1.83^{ax} \pm 0.06$	$1.38^{y} \pm 0.06$

a-b : Values bearing same superscript in a column did not differ significantly.

x-z : Values bearing same superscript in a row did not differ significantly.

Table - 10A

Analysis of variance for the effect of anaesthetic agents on creatinine (mg%) in goats.

Period	Source of Variation	df.	M.S.	F.
0 Hr.	Between groups	2	0.04	3.30^{NS}
	Error	12	0.01	
1 Hr.	Between groups	2	0.17	17.5**
	Error	12	0.01	
2 Hrs.	Between groups	2	0.32	29.54**
	Error	12	0.01	
3 Hrs.	Between groups	2	0.34	28.66**
	Error	12	0.01	
24 Hrs.	Between groups	2	0.04	3.75^{NS}
	Error	12	0.01	

** = Significant at ($p<0.01$)

Table - 10 B

Analysis of variance for the effect of anaesthetic agents on creatinine (mg%) in goats.

Group	Source of Variation	df.	M.S.	F.
Group I	Between periods	4	0.012	2.17^{NS}
	Error	20	0.005	
Group II	Between periods	4	0.050	2.93*
	Error	20	0.017	
Group III	Between periods	4	0.218	14.84**
	Error	20	0.014	

NS = Non-significant

*** = Significant at ($p<0.05$)**

*** = Significant at ($p<0.01$)**

CHAPTER - V

DISCUSSION

CHAPTER - V

DISCUSSION

DISCUSSION

Clinical Parameters :

Rectal Temperature :

The clinical observation revealed that administration of xylazine (group–I) and ketamine (group-II) had little or no effect on the body temperature. Kumar and Thurmon (1979) reported a slight decrease of rectal temperature in goats. Similar findings were also reported by Pratap *et al.* (1998) in buffalo calves and Varshney (1998) in Ponies. The fall in rectal temperature might be related to central α_2 adrenergic mechanism (Livingston *et al.,* 1984). In group III, (xylazine and ketamine combination), slight decrease was marked at 45 to 75 minutes of induction. Similar findings were reported by Kumar and Singh,(1979) in bovine; Kumar, *et al.,* (1983) in goats. Wyk and Bery (1986) in lions and Kinjavdekar *et al.,* (1997) in goats after the use of xylazine and ketamine combination. However, a significant decrease was observed by Kumar *et al.* (1979) in canine, Samy *et al.* (1982) in ovine, Chitale *et al.* (1998) and Ekka *et al*, (1996) in caprine.

Pulse rate :

The animals of the different groups showed variant pattern in the manifestation of the pulse rate with xylazine, ketamine and their combination. In group I (xylazine), the pulse rate showed a significant decrease when administered alone. This decrease was more marked after 15 minutes of induction. The same pattern of pulse rate was also reported by Tantaway *et al.* (1982) in buffaloes, Sharma, *et al.* (1983) in horse, Fayed *et al.* (1989) in heifers and Varshney (1998) in Ponies.

In group II and III, pulse rate showed a significant increase after induction of ketamine and xylazine-ketamine combination. In group II, an

increase in pulse rate was marked from 15 minutes onwards till 105 minutes and there after it was nearer to normal level. Similarly in group III, an increase in pulse rate was marked from 20 minutes onwards then gradual discrease was marked upto 120 minutes of experiment. It was also observed that the pulse rate did not increase up to the level induced by ketamine alone. Which might be due to the parasympathomimetic action of xylazine as had been reported by Kumar *et al.*, (1983). Decrease in pulse rate had also been recorded by Waterman (1981) in calves, Samy *et al.* (1982) in sheep and Oeppert (1973) in cats.

Respiration rate :

The respiration rate significantly decreased in group I and increased in group II and III. In group I, the decrease of respiration rate started from 5th minute onwards and remained till 90 minutes and thereafter a gradual increase was marked which was nearer to the normal level in 120 minutes of experiment. This decrease in respiration rate after xylazine administration might be due to direct depression of respiratory centre as has been reported by Kumar and Thurmon (1979). Similar findings were also reported by Kumar *et al.* (1976) in buffaloes, Kumar and Singh (1976) in cattle, Waterman *et al.* (1987) in sheep, Jean *et al.* (1990), Skarda *et al.* (1990), Rehage *et al.* (1994) in cattle, Kinjavdekar *et al.* (1998) and Aithal *et al.* (1997) in goats.

In group III, when ketamine was administered alone there was significant increase in respiration rate. The significant increase in respiration rate started from 15 minutes onwards and remained increased till 120 minutes of experiment. An increase in respiration rate might be due to the stimulatory effect of ketamine on the respiratory centres. It has also been

reported due to residual action of ketamine as the latter stimulated certain subcortical areas of the C.N.S. which has been observed by Wright (1982). Similar observations were also reported by Kumar *et al.* (1983-86) and Islas *et al.* (1985).

In group III, a significant increase in respiration rate was recorded from 15 minutes onwards till 90 minutes and thereafter gradual decrease was observed nearer to normal level after the use of xylazine-ketamine combination. This increased respiration might be due to predominant effect of ketamine and its stimulatory effect might had balanced the depressant actions of xylazine. Depression in respiratory action in the latter stages might be due to the depressant action of xylazine as by that time the action of ketamine would have disappeared. It has also seen reported that there was decrease in respiratory rate after systemic administration of ketamine and xylazine in dogs. (Moens and Fregetton, 1990). Similar findings were recorded by Wyk and Berry (1986) in lions and White *et al.* (1987) in domesticated dromedary (camel).

ANAESTHETIC PARAMETERS :

Onset of action :

Clinical observation revealed production of tranquilisation and analgesia simultaneously among the experimental goats in each group. The loss of various reflexes were quite variable and sometime quite unpredictable in all the groups. The early onset of action was recorded by the combination of xylazine and ketamine (group III) followed by xylazine (group I) and lastly by ketamine (group II). In group I, onset of action was quicker than group II. It was perhaps due to large dosages of xylazine (0.4 mg/kg) as xylazine is known for dose dependent sedative anaesthetic agent. The same

finding was observed by Hopkins (1972) in cattle where a small dose of xylazine produced rapid onset of dose dependent sedation analgesia and muscle relaxation.

Administration of ketamine at the dose rate of 12 mg/kg intramuscularly produced a state in which animal appeared disconnected rather than in asleep. Auditory reflex was present. The normal muscle tone and other reflexes were observed throughout the observation period. Similar findings were also observed by Humphrey (1971). It has also been suggested by Hoeppner and Short (1971) that ketamine had a rapid action in addition to safe and satisfactory anaesthesia.

The xylazine-katamine combination produced early onset of action in comparison to xylazine and ketamine alone. Xylazine produced a depression of central nervous system as a result of which there was a very good relaxation and animal appeared to be sleepy in xylazine-ketamine anaesthsia. In an earlier experimental endeavour, it had been observed that during ketamine anaesthesia, laryngeal and pharyngeal reflexes remained present in goats (Kumar *et al.,* 1976). It might be due to the predominant local anaesthetic effect of ketamine in comparison to α_2 agonist (Le Blanc *et al.,* 1988). In xylazine-ketamine combination quick onset of action was also reported by Pandey *et al.* (1996) in horse and Aithal *et al.* (1997) in goats.

Combination of xylazine with ketamine (group III) produced analgesia for longer duration as compared to that of xylazine (group I) and ketamine (group II) where drugs were used alone. It has been observed that for prolong surgery, combination of xylazine-ketamine was suitable and produced deep state of anaesthesia and good analgesia in goats (Keller and Bauman, 1978). Similar observations were also reported by Amend *et al.*

(1972) in cats, Kumar and Singh, (1979) in bovine calves, Singh *et al.* (1985) in buffaloes, Aithal *et al.* (1997) in goats and pratap *et al.* (1999) in baffalo calves.

The recovery periods in the individual animal of all the groups were variable and differed significantly within the group. The order of recovery was earliest in ketamine followed by xylazine and xylazine-ketamine combination. Early recovery in ketamine and xylazine alone in comparison to the combination group might be due to the fact that the combination of two drugs used in the study might have acted synergistically to produce a longer duration of action (analgesia) and sedation and have delayed recovery. It has been suggested that the combination of xylazine-ketamine was used for prolong surgery in goat which produced deep state of anaesthesia and good analgesia for period of long duration (Keller and Bauman, 1978). No mortality could be detected during the period of observation and uneventful recovery was marked in all the goats, which indicated that the analgesia and sedation produced reasonable safety margin in the dose evaluated in this study. Therefore, it is explicit that combination group produced superior degree of anaesthesia as compared to xylazine and ketamine alone and could be employed in animal having poor physical state.

Frequent urination was observed in most of the animals after administration of xylazine alone and in combination with ketamine during variable time span within observation periods. This might be due to inhibition of production and release of ADH. Salivation was uniformly observed but of no clinical significant. Salivation was scanty in group II than group I and III. This corroborate with the earlier findings with xylazine in dogs (Ramaswamy *et al.,* 1991). Marked salivation and vocalization had

been exhibited in xylazine administered calves (Raidurg and Ranganath 1994). Defecation was absent in all the groups.

Analgesia

Analgesia was recorded by using 0 – 3 scale to pin-prick response at anterior and posterior flank including ear, thorax, tail and digits. No analgesia, mild analgesia, moderate analgesia and strong/complete analgesia were observed in all the groups. More longer duration of action was observed in group III followed by group I and II. It might be due to the fact that concentration of xylazine was more in group III and I. It has been suggested that xylazine had local anaesthetic effect and produced analgesia probably by stimulation of α_2 adrenoreceptors in spinal cord and CNS, thereby inhibiting the release of neurotransmitters and decreasing neuronal activity (Aziz and Martin, 1978; Kuruishi *et al.,* 1985 and Le Blane *et al.,* 1988).

In group II, mild to moderate analgesia with shorter duration was observed. This findings was also observed by Keller and Bauman (1978) in goats.

It is obvious after observing the analgesia on 0 – 3 scale that it was satisfactory to excellent, the latter was achieved in combination of xylazine and ketamine. The synergistic action of two anaesthetic agents might be the main factors which contributed toward excellent analgesia. Xylazine in combination with ketamine produced a longer duration of anesthesia in comparison to xylazine or ketamine alone. It might be due to synergistic interaction between xylazine and ketamine. Similar findings had been reported by Amarpal *et al.* (1997) in cattle.

Sedation :

Following systemic administration of anaesthetic agents sedation was observed in group I, II and III. Moderate sedation was observed within 3 to 5 minutes after intramuscular administration of xylazine and then sedation continued upto 55 to 65 minutes. In this stage animal appeared tired which was indicated by drooping of head and eye lids and observed in recumbent position. The sedative action of xylazine is assocated with the stimulation of α_2 adrenoreceptors which causes in the release and turn over of norepinephrine in the CNS. The onset of sedation started latter than the onset of analgesia after drug administration. This indicates that analgesic effects of anaesthetic agents is mediated by spinal action rather than central effect. It has been suggested that a dose dependent sedative had been reported caudal epidural administration of α_2 agonists (xylazine) owing to their central α_2 adrenergic effects in cow (Skarda *et al.,* 1989). Xylazine produced mild to moderate sedation after epidural administration in mares (skanda and Muir, 1996) and goats (Aithal *et al.*, 1997).

After administration of ketamine alone, mild sedation started within 5 to 7 minutes and continued upto 25 to 35 minutes. However, analgesia with mild sedative effects of ketamine was reported by Ravat *et al.* (1987) and it could be explained by vascular uptake of ketamine from the epidural space and the development of systemic effects.

In group III, satisfactory and excellent sedation was observed. The development of sedation was earlier and continued for the longest period. The sedation was observed from 2.30 to 3.30 minutes of induction and it continued beyond 85 minutes. In this group, animal remained in lateral recumbency from 3 to 85 minutes. Sedation produced in group III might be

manifestation of central effects of xylazine and its potentiation by the combination of ketamine. The degree of sedation produced by xylazine in combination with ketamine was greater in comparison to that produced by xylazine and ketamine alone. It has also been reported that ketamine and xylazine combination produced excellent analgesia of flank, thorax ventral abdomen and hind limbs used at the first lumbar epidural space in goats (Kinjavdekar *et al.*, 1997).

Reflexes :

Different reflexes like corneal, palpebral and pedal were studied after administration of anaesthetic agents. Absence of painful stimuli was obtained by lifting the site with Allis tissue forceps and deep pin-priks for assessment of the depth of anaesthesia. It was satisfactory and excellent in group III followed by group I and II.

Biochemical Studies :

Blood glucose value in in the present study revealed hyperglycaemic feature in all the groups. The magnitude of rise in glucose level was greater in group III as compared to the other two groups. All the group showed marked elevation in the glucose level during 1 to 3 hours of drug administration and normalizing trend at 24 hours. Thus, the observations made for blood glucose level was also in agreement with result of Kumar and Singh (1976) in cattle, Kumar and Singh (1978) in horse, Kumar and Thurmon (1979) in goat, Eichner *et al.* (1979) in cattle, Amer and Misk (1980) in goats, Brockman (1981-82) in sheep, Peshin and Kumar (1983) in buffaloes, Fayed *et al.* (1989) in heifers, Phode and Aher (2003) in bovine after systemic administration of xylazine alone. Similarly an increase in blood glucose level was recorded after ketamine administration. The same

findings were also reported by Kumar and Thurmon (1974) in sheep, Kumar *et al.* (1985) in goats, Kelawala *et al.* (1991), Singh *et al.* (1999) and Kinjavdekar (2001) in goats.

When xylazine and ketamine combination was administered systematically, an increase in blood glucose level was observed alike xylazine and ketamine alone. These findings corroborate the observation of Kumar and Singh (1979) in bovine, Kumar *et al.* (1979) in dogs, RamaKrishna *et al.* (1981) in buffaloes, Ekka *et al.* (1996) in goats, Chitale *et al.* (1999) and Kinjavdekar (2001) in goats after the use of xylazine-ketamine combination. Hyperglycaemic effect might be due to an α-adrenergic inhibition of insulin released by stimulation of α_2-receptors in the pancreatic β-cells (Angel and Langer, 1988) and to an increased glucose production in the liver (Brockman, 1981).

The alterations in blood urea nitrogen fluctuated within the normal physiological level with marginal increase at 1 and 2 hours in all the groups. Phode and Aher (2003) reported a non significant rise in blood urea nitrogen level at maximum depth of sedation and anaesthesia in bovine after xylazine administration. Similar observations were made by Mottelib and Gindi (1975) in buffloes, Echner *et al.* (1979) in cattle and Amer and Misk (1980) in goats and marked temporary increase in the level of blood urea nitrogen.

A non significant increase in blood urea nitrogen has been described by Kelawala *et al.* (1991) due to fasting of animal and mild depression of kidney function during use of ketamine anaesthesia in goats. Mild change in blood urea nitrogen level which fluctuated within the normal physiological range after systemic administration of ketamine has also been reported by Singh *et al.* (1999) in caprine. While Singh *et al.* (1985) observed no

alteration in blood urea nitrogen level after administration of xylazine-ketamine combination in buffaloes. However, a marked elevation was recorded by Samy *et al.* (1982) in sheep, More *et al.* (1993) in cow calves and Kinjavdekar (2001) in goats after administration of xylazine–ketamine combination.

The serum creatinine showed non significant changes in all three groups. These findings corroborate the observation of Hussain and Kumar (1988) who had used xylazine in buffaloes, Singh *et al.* (1985) with xylazine-ketamine anaesthesia in buffaloes and Kelawala *et al.* (1991) with diazepam-ketamine anaesthesia. However, a marginal alteration in the creatinine level in goats was recorded after xylazine administration. These light variations were probably inconsequential as has been reported by Kumar and Thurmon (1979). Similar findings were also reported by Mottelib and Gindi (1975) and Kinjavdekar (2001) in caprine after the use of xylazine.

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CHAPTER - VI

SUMMARY AND CONCLUSION

SUMMARY AND CONCLUSIONS

Xylazine and ketamine were evaluated alone and in combination as a general anaesthetic in 15 clinically healthy non-descript she goats, aging one to two and half years. and weighing in between 12-20 kg. The animals were randomly divided into three groups having five animals in each group. Xylazine and ketamine were injected alone and in combination at a dose rate of 0.4 mg, 12 mg and 0.4 + 12 mg per kilogram body weight intramuscularly in respective groups. The observations were made on the basis of rectal temperature, pulse rate, respiration rate, onset of action, duration of action, recovery period, different reflexes like corneal, palpebral, cutaneous and pedal, sedation, extent and magnitude of analgesia. Sedation was judged by recording drowsiness, lowering of head and its posture.

Biochemical examinations included estimation of glucose, urea nitrogen and creatinine in blood. The observation which could be made and the result obtained during the present study revealed that all these anaesthetics are worthy to use in caprine but the actions of ketamine is mild and transient, while the action of xylazine is moderate which can be used for surgery, but a combination of xylazine and ketamine is more suitable to use as anaesthetic effect remains for a longer duration with good muscle relaxation. There was lack of any type of post anaesthetic complications or death after anaesthesia in any group. Details of anaesthetic methods, observations and results of the present study are discussed.

On the basis of observations made during the present study following conclusions are drawn :

1. Xylazine alone produced deep sedation and optimal muscle relaxation in goats.
2. Ketamine alone produced optimal sedation and analgesia for a short duration (only for 25-35 minutes) but inadequate muscle relaxation in the goats.
3. When the combination of xylazine and ketamine were administered, there was excellent analgesia, deep sedation adequate muscle relaxation and abolition of superficial and deep cutaneous reflexes permitting for clinical surgery when needed.
4. Xylazine alone and in combination with Ketamine did not exhibit any biochemical change during the observation after its medication.
5. Moderate hyperglycaemia was observed during study after the use of Ketamine alone. Thus, the use of xylazine and Ketamine in combination was suitable wherever needed prior to surgery in caprine as compared to xylazine and ketamine alone.

In authors opinion, ketamine, xylazine and their combination are suitable to use in caprine clinically for small, moderate and large duration surgery wherever needed.

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BIBLIOGRAPHY

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Ahuja, B.R. (1983). Analgesic effects of intrathecal ketamine in rats. *Br. J. Anaesth.*, **55** : 991-995.

Aithal, H.P., Amarpal, Kinjavdekar, P. and Singh, G.R. (1997). Epidural anaesthesia with ketamine in poor risk surgical patients (In press).

Aithal, H.P., Amarpal, Pratap, K. and Singh, G.R. (1994). Epidural xylazine and ketamine for hind quarter analgesia in goats. Paper presented in 18th Annual Congress of I.S.V.S., Tirupati, Sept. p. 709, 1994.

Aithal, H.P., Amarpal, Pratap, K. and Singh, G.R. (1997). Clinical effects of epidurally administered ketamine and xylazine in goats. *Small Rum. Res.*, **24** : 55-64.

Aithal, H.P., Amarpal., Singh, G.R., Mogha, I.V., Gupta, O.P., Kumar, N. and Hoque, M. (1997). Epidural ketamine and xylazine for hind quarter surgery in ruminants, a study on 35 clinical cases. *Indian Vet. J.* **74** : 7, 625-626.

Amarpal, Aithal, H.P., Kinjavdekar, P. and Singh, G.R. (1998). Effects of epidural ketamine and pethidine in dogs. *Indian J. Vet. Surg.*, **19** : 62.

Amarpal, Aithal, H.P., Singh, G.R., Pawde, A.M. and Sharma, A.K. (1997). Epidural xylazine and ketamine for hind quarter analgesia in cow calves. *Indian J. Anim. Sci.*, **67** : 587-588.

Amend, J.F., Klavano, P.A. and Stone, E.C. (1972). Premedication with xylazine to eleminate muscular hypertonicity in cats during ketamine anaesthesia. *Vet. Med. Small Anim. Clin.* **67** : 1305-1308.

Amer, A.A. and Misk N.A. (1980) Rompun in goats with special reference to its effect on the cerebrospinal fluid. *Vet. Med. Rev.* : 168-174.

Angel, I. and Langer, S.Z. (1988) Adrenergic induced hyperglycaemia in anaesthetized rats. *European J. Pharmacol.* **154** : 191-196.

Aziz, M.A. and Martin, G.J. (1978). Alpha agonist and local anaesthetic properties of xylazine. *Zb. Vet. Med.* **25** : 181-188.

Balakishan, K. and Rao, R.L.N. (1993). Epidural analgesia with xylazine and lignocaine HCl in buffalo calves. *Indian J. Vet. Surg.* **14** : 50.

Barbalia, D.R., Patil, D., Kelawala, N.H., Parikh, P.V., Parasama, R.R. and Sonwane, N.A. (1998). Comparative study of lignocaine, ketamine and ketamine-lignocaine combination for epidural analgesia in goats. *Indian Vet. Med. J.* **22** : 317-320.

Berlinger, R. and Lakatos, L. (1972). Ketalar (Ketamine HCl) for the tranquilization of cats. *Schweizer Archivefur Tierheilkunde.* **10** : 488-496

Bion, J.E. (1984). Intrathecal Ketamine for war surgery. A preliminary study under field conditions. *Anaesthesia*, **39** : 1023-1028.

Brockman, R.P. (1981). Effect of xylazine on plasma glucose, glucagon and insulin concentration in sheep. *Res. Vet. Sci.* **30** : 383-384.

Chiasson, R.B., Egge, A.S. and Lynch, B. J. (1973). The effect of Ketalar on the adrenal gland of young White Leghorn Cockerels. *Poult. Sci* **52** : 1014-1018.

Chitale, D., Pratap, K., Amarpal, Singh, G.R., Pawde, A.M. and Gupta, O.P. (1998). Alpha-2 agonists with diazepam as preanaesthetics to ketamine anaesthesia in goats: physiological and haematological study. *Indian J. Vet. Surg.* **19** : 103-104.

Chitale, D., Pratap, K., Amarpal, Singh, G.R. and Gupta, O.P. (1999). Biochemical effect of ketamine with premedication of alpha-2 agonists and diazepam in goats. *Ind. Vet. J.* **76** : 304-305.

Compbell, K.B., Klavano, P.A., Richardson, P. and Alexander, J.E. (1979). Haemodynamic effects of xylazine in the calf. *Am.J. Vet. Res.* **40** : 1777-1780.

De young, D.W. (1972). Dissociative anaesthetic in cat and dog. *J. Am. Vet. Med. Assoc.* **161** : 1442-1445.

Dhasmana, K.M., Salt, P.J., Faithfull, N.S. and Erdmann, W. (1986). Effect of intrathecal and intracarotid administration of ketamine on blood pressure and heart rate in rats. Arch. *Pharmacodyn. Ther.* **280** : 95-105.

Doiphode, P.V. and Aher, V.D. (2003). Haematological and bio-chemical effects of neuroleptanalgesia with xylazine and pentazocine in bovine. *Indian Vet. J.*, **80** : 775-777.

Eichner, R.D., Proir, R.L. and Krasenicka, W.G. (1979). Xylazine induced hyperglycaemia in Beef cattle. *Am. J. Vet. Res.*, **40** : 127-129.

Ekka, L.K. Dass, L.L. Sahay, P.N. and Paul, A.K. (1996). Certain biochemical changes induced by different ketamine combinations in atropinised goats. *Indian Vet. J.* **73** : 784-785.

Fayed, A.H., Abdalla, E.B., Anderson, R.R., Spencer, K. and Johnson, H.D. (1989). Effect of xylazine in heifers under thermoneutral or heat stress conditions. *Am. J. Vet. Res.* **50** : 151-153.

Hoeppener, G.L. and Short, C.E. (1971). Ketamine : A new anaesthetic for cats. *Southwest Vet.* **24** : 175-182.

Hopkins, T.J. (1972). The clinical pharmacology of xylazine in cattle. *Australian Vet. J.* **48** : 109-112.

Hsu, W.H. (1981). Xylazine-induced depression and its antagonism of alpha adrenergic blocking agents. *J. Pharmacol. Exp. Ther.* **218** : 188-192.

Humphrey, W.J. (1971). Ketamine HCl as a general anaesthetic in dogs. *Mod. Vet. Pract.* **52** : 38-39.

Hussain, S.S. and Kumar A. (1988). Tachyphylaxis to epidural anaesthesia in buffaloes. *Ind. J. Ani. Sc.* **58** : 2, 182 – 188.

Islas, J.A., Astorga, J. and Laredo, M. (1985). Epidural ketamine for control of post-operative pain. *Anaesth. Analg.* **64** : 1161-1162.

Ivankovitch, A.D., Miletich, D.J., Reinman, C.N., Albrecht, R.F. and Zahel, B. (1974). Cardiovascular effects of centrally administered ketamine in goats. *Anaesth. Analg.* **53** : 924-933.

Jean, G.St., Skarda, R.T., Muir, W.W. and Hoffsis, G.F. (1990). Caudal epidural analgesia induced by xylazine administration in cows. *Am. J. Vet. Res.* **51** : 1232-1236.

Kelawala, N.H., Parsania, R.R. and Patil, D.B. (1991). Haematological and biochemical studies on ketamine, propofol and propofol – ketamine as general anaesthesia in diazepam premedicated goats (Capra hircus). *Ind. J. Vet. Surg.* **12** (1) 17 – 20.

Kelawala, N.H. and Parsania, R.R. (1992). Preliminary studies on propofol, ketamine and propofol-ketamine anesthesia in diazepam premedicated goats (*Capra hircus*) phsiological profiles, *Ind. Vet. J.* **69** : 725-729.

Keller, G.L. and Bauman, D.H. (1978). Ketamine and xylazine anaesthesia in goats. *Vet. Med. Sm. Anim. Clin.* **73** : 443-444.

injavdekar, P. (1998). Spinal analgesia with α 2-agonists and their combinations with ketamine and lignocaine in goats. Ph.D. Thesis submitted to I.V.R.I., Deemed University, Izatnagar (U.P.), India.

injavdekar, P., Aithal, H.P., Amarpal, Hoque, M. and Pratap, K. (1997). Lumber epidural anaesthesia with ketamine and xylazine in goats. *Indian J. Vet. Surg.* **18** : 56.

night, A.P. (1980). Xylazine. *J. Am. Vet. Med. Assoc.* **176** : 454-455.

injavdekar, P., Singh, G.R. and Amarpal (1999). Alpha 2 agonists for spinal analgesia in animals : A review. *Indian J. Vet. Surg.* **20** : 1-9.

injavdekar, P. and Singh, G.R. (2001). Effect of spinally administered ketamine alone and its combination with xylazine and medetomidine in goats. Abstract. 25th I.S.V.S., Annual Conference. pp. : 7.

umar, A., Pandey, S.K., Chandrapuria, V.P. and Sharivastava, S.M., (1986). A note on clinical evaluation of different ketamine combination in goats. *Indian J. Vet. Surg.* 7 : 65-67.

umar, A. Pandey, S.K. Chandrapuria, V.P. and Shrivastava, S.M. (1985). Haematological and biochemical evaluation of different ketamine combinations in goats. *Indian J. of Anim. Sci.* **55** : 106-107.

umar, A., Pandiya, S.C. and Singh, H. (1979). Canine anaesthesia with a combination of ketamine and xylazine in experimental and clinical cases. *Indian. J. Anim. Health.* **18** : 39-43.

mar, A. and Singh, H. (1976). Xylazine as an immobilizing agent in cattle. *Indian. Vet. J.* **53** : 799-803.

mar, A. and Singh, H. (1978). Xylazine as a sedative and analgesic agent in equine surgery. *Indian. J. Anim. Hlth.* **17** : 7-11.

Kumar, A. and Singh, H. (1979). Ketamine and xylazine anaesthesia in bovine paediatric surgery. *Ind. Vet. J.* **56** : 219-222.

Kumar, A., Thurmon, J.C. and Dorner, J.L. (1974). Haematological and biochemical findings in sheep given ketamine hydrochloride. *J. Am. Vet. Med. Assoc.* **165** : 284-287.

Kumar, A., Thurmon, J.C. and Hardenbrook, H.J. (1976). Clinical studies of ketamine HCl and xylazine HCl in domestic goats. *Vet. Med. Sm. Anim. Clin.* **71** : 1707-1713.

Kumar, A. and Thurmon, J.C. (1977). A note on anaesthetic effects of mixture of acepromazine and ketamine hydrochloride in goats. *Indian J. Anim. Sci.* **47** : 601-604.

Kumar, A. and Thurmon, J.C. (1979). Cardiopulmonary haematocytogenic and biochemical effects of xylazine in goats. Lab. *Anim. Sci.* **29** : 486-491.

Kumar, A., Thurmon, J.C., Nelson, D.R., Benson, G.J. and Tranquilli, W.J. (1983). Response of goat to ketamine hydrochloride with and without premedication of atropine, acetylpromazine, diazepam and xylazine. *Vet. Med. Small Anim. Clin.* 79 : 955.

Kuruishi, Y., Hirota, N., Sato, Y., Kaneko, S., Satoh, M. and Takagi, H. (1985). Noradrenergic inhibition of the release of substance P from the primary afferents in the rabbit spinal dorsal horn. *Brain Res.*, **359** : 117-182.

Lacuata, A.Q. and Leon, D.A. (1973). A preliminary study on the sedative effects of Rompun in cats. *Philippine J. Vet. Med.* **11**(2) : 134-146.

Lanning, C.F. and Harmel, M.H. (1975). Ketamine anaesthesia *Annu. Rev. Med.*, **26** : 137-141.

Le Blanc, P.H. and Cardon J.P. (1990). Clinical use of epidural xylazine in the horses. *Equine Vet. J.*, **22** : 180-181.

Le Blanc, P.H., Cardon J.P., Patterson, J.S., Brown, M. and Matta, M.A. (1988). Epidural injection of xylazine for perineal analgesia in horses. *J. Am. Vet. Med. Assoc.*, **193** : 1405-1408.

Lin, M.T., Chen, C.F. and Pang, I.H. (1978). Effect of ketamine on thermoregulation in rats. *Can. J. Physiol. Pharmacol.*, **56** : 963-967.

Livingston, A., Low, J. and Morris, B. (1984). Effects of clonidine and xylazine on body temperature in the rat. *Br. J. Pharmacol.*, **18** : 189-195.

Moens, Y. and Fregetton, X. (1990). A comparative study of medetomidine/ketamine and xylazine/ketamine anaesthesia in dogs. *Vet. Rec.* **127** : 567-571.

More, D.B., Bhokre, A.P. and Aher, V.D. (1993). Experimental evaluation of Diazepam-xylazine ketamine anaesthesia in cow calves-II (Biochemical and Haematological study). *Indian. Vet. J.* **70** : 348-350.

Muggaberg, J. and Brockman, R.P. (1982). Effect of adrenergic drugs on glucose and plasma glucagon and insulin responses to xylazine in sheep. *Research in Vet. Sci.* **1** : 118- 120.

Nolan, A., Livingston, A. and Waterman, A. (1987). Antinociceptive action of intravenous α 2-adrenoceptor agonist in sheep. *J. Vet. Pharmacol. Ther.*, **110** : 202-209.

Oeppert, G. (1973). Anaesthesia of cats with ketamine xylazine with special reference to respiratory and circulatory effects. Kreislaufbeeinflussung inaugural Dissertation, *Tierarztliche Fakultat* : Muchen. pp. 112.

Panday, S.S., Singh, V. and Shukla, B.P. (1996). Evaluation of xylazine and ketamine hydrochloride with and without diazepam inequines. *Indian. J. Vet. Surg.* **17** : 120-121.

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

Ponder, S.W. and Clark, W.G. (1980). Prolonged depression of thermoregulation after xylazine administration to cats. *J. Vet. Pharmaco. Ther.* **3** : 203 – 207.

Pratap, K., Amarpal and Kinjavdekar, P. (1998). Epidural xylazine in buffalo calves. *Indian J. Vet. Surg.* **19** (1) : 60.

Pratap, K., Kinjavdekar, P. and Amarpal (1999). Lumbosacral epidural analgesia with xylazine and ketamine in buffalo calves. *Indian Vet. Surg.*, **20** : 109.

Raidurg, R. and Ranganath, B.N. (1994). Study of xylazine as an epidural analgesic in experimental calves. *Indian J. Vet. Surg.*, **15** : 58.

Ramakrishna, O., Krishna murthy, D. and Nigam, J.M. (1981). Ketamine anaesthesia in buffalo calves. *Indian. Vet. J.* **58** : 503-505.

Ramaswamy, V., Balasubramaniam, N.N., Gopal, M.S. and Archibald, D. (1991). Studies on the efficacy of ketamine hydrochloride as general anaesthetic in combination with xylazine, diazepam and promazine in canines (qualitative changes). *Indian Vet. J.* **68** : 439-442.

Ravat, F., Dorne, R., Baechle, J.P., Beaulaton, A., Leoir, B., Leroy, P. and Palmier, B. (1987). Epidural Ketamine or morphine for post operative analgesia. *Anaesthesiol.*, **66** : 819-822.

Reddy, G.S., Anadarao, K., Ramarao, K., Kalanidhi, A.P. and Srinivasan, V.A. (1991). Use of xylazine in cattle. *Indian. Vet. J.* **68** : 418-420.

Rehage, J., Kehler, W. and Schloz, H. (1994). Use of xylazine for epidural anaesthesia in cattle. Deutsche, Tierarztli. **101** : 14-16.

Reibold, T.W. Grubb, T.L. and Crimson, R.O. (1992). Comparision of lignocaine, xylazine and lignocaine xylazine for epidural anaesthesia in cattle (Abstr.) *Vet. Surg.* **21** : 159.

Samy, M.T., Tantawy, M., Ibrahim, H. and Mothelib, A.A. (1982). Studies on the clinical application of combined vetalar-Rompun in sheep. *Assiut Vet. Med. J.* **9** : 143-146.

Shokry, M., Morad, H.M. and Khalil, I.A. (1976). Studies on the effect of Rompun (xylazine) in sheep. *Vet. Med. Review* 237-243.

Singh, A.P., Jit, Singh., Peshin, P.K., Gahlawat, J.S., Singh, P., Nigam, J.M. (1985). Evaluation of xylazine-ketamine anaesthesia in buffaloes (*Bubalus bubalis*). *Zentralblatt-fur-veterinarmedzin*,-A. **32** : 54-58.

Singh, S.K., Sahay, P.N. and Gupta, M.K. (1999). Biochemical alterations induced by ketamine and its combination with diazepam and lorazepam in goats. *Indian Vet. J.*, **76** : 896-897.

Skarda, R.T. and Muir, W.W. (1992). Physiologic responses after caudal epidural administration of detomidine in horses and xylazine in cattle. Animal pain. 1st edn. pp. 292-302.

Skarda, R.T. and Muir, W.W. (1996) Analgesic haemodynamic and respiratory effects of caudal epidurally administered xylazine hydrochloride solution in mares. *Am. J. Vet. Res.*, **57** : 193-200.

Skarda, R.T., Jean, G. and Muir, W.W. (1989). Influence of caudal epidural xylazine on central nervous, respiratory cardiovascular and reticuloruminal motor function in cows. *Vet. Surg.*, **8** : 249.

Skarda, R.T. St. Jean, G. and Muir W.W. (1990). Influence of tolazoline on caudal epidural administration xylazine in cattle. *Am. J. Vet. Res.*, **51** (4) : 556 – 560.

Strub, O.C. (1971). Rompun (Xylazine) anaesthesia in sheep. *Deutsche Tierarztliche Wochenschrift*, **78** : 537-538.

Thurmon, J.C., Kumar, A. and Link, R.P. (1973). Evaluation of ketamine hydrochloride as an anaesthetic in sheep. *JAVMA*. **162** : 293-297.

Varshney, J.P. (1998). Clinical evaluation of xylazine hydrochloride in healthy ponies. *Indian J. Vet. Surg.*, **19** : 44.

Vicente, W.R.R., Toniollo, G.H. and Laus, J.L. (1987). Observations on combination of ketamine and xylazine for anaesthesia of sheep. *Ars. Veterinaria*, **3** : 211 – 217.

Vigo, D., Rensis, F.D.E., Ramella, F. and Maffeo, G. (1989). Preliminary observations on dissociative anaesthesia (Xylazine-Ketamine) in pigs. *Selezoine Veterinaria*. **30** : 1697-1701.

Waterman, A.E. (1981). Preliminary observations on the use of a combination of xylazine and ketamine hydrochloride in calves. *Veterinary record* **109** : 464-467.

Waterman, A.E. and Livingston, A. (1978). Some physiological effects of ketamine in sheep. *Res. Vet. Sci.*, **25** : 225-233.

Waterman, A.E., Livingston, A. and Bouchenafa, O. (1987). Analgesic effects of intrathecally applied α2-adrenoceptor agonists in conscious, unrestrained sheep. *Neuropharmacol.*, **27** : 213-216.

Waterman, A.E., Livingston, A., Bouchenafa, O. and Dagh, L. (1988). Analgesic actions of α2-adrenoceptor agonist drugs administered

intrathecally in conscious sheep (Abstr.). In proceedings third International Congress of Vet. Anaesth. Brisbane, Australia.

White, R.J., Bali, S. and Bark, H. (1987). Xylazine and ketamine anaesthesia in the dromedary camel under field conditions. *Vet. Rec.* **120** : 110-113.

Wyk, T.C. VAN. and Berry, H.H. (1986). Tolazoline as an antagonist in free living lions immobilized with a ketamine-xylazine combination, *Jour. of the South African Vet. Assoc.* **57** : 221-224.

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