"Comparative studies on the effect of diazepam as preanesthetic during α-2 agonist (xylazine) and ketamine anesthetic alone and in combination 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

(VETERINARY SURGERY & RADIOLOGY)

By

DR. NARENDRA TIWARI

Registration No. M/VSR/64/2004-2005

DEPARTMENT OF VETERINARY SURGERY & RADIOLOGY
BIHAR VETERINARY COLLEGE
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CERTIFICATE- I

This is to certify that thesis entitled *"COMPARATIVE STUDIES ON THE EFFECT OF DIAZEPAM AS PREANAESTHETIC DURING ALPHA- 2 AGONIST (XYLAZINE) AND KETAMINE ANAESTHETIC ALONE AND IN COMBINATION IN CAPRINE"* submitted in partial fulfillment of the requirements for the Degree of **Master of Veterinary Science (Veterinary Surgery and Radiology)** of the Faculty of post-graduate studies, Rajendra Agricultural University, Pusa, Samastipur, Bihar is the record of bonafied research work carried out by **Dr.Narendra Tiwari**, Admission No. VP/BVC/VSR-01/2004-2005 Registration No. M/VSR/64/2004-2005, 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.

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We, the undersigned members of the Advisory Committee of **Dr. Narendra Tiwari**, Registration No. M/VSR/64/2004-2005, 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 DIAZEPAM AS PREANAESTHETIC DURING ALPHA- 2 AGONIST (XYLAZINE) AND KETAMINE ANAESTHETIC ALONE AND IN COMBINATION IN CAPRINE*" may be submitted by **Dr. Narendra Tiwari** in partial fulfillment of the requirements for the degree.

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Place: Patna

Date: 23-10-06

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INTRODUCTION

Agriculture has an important role to play in the fast growing Indian economy. Being complementary to the agricultural activities Animal Husbandry sector along with the livestocks constitute about 30 percent of country's agricultural output, where as, it alone contribute 10 percent(Mehta et al. 2002) to the Gross Domestic Product (GDP) in India.

Goat being the earliest prehistoric discovery of mankind is one of the important livestock, which has been regarded as "poor men's cow". They have some excellent merits to be reared at extensive (zero) management as well as the efficient converter of the low quality forages into the high quality products like meat, milk, hide etc. Although goats are well adapted to the Indian climate, however in the field conditions lots of clinical cases are prevalent where surgical interventions are needed.

Satisfactory anesthesia for the performance of painful surgical interferences on animals is essential from two stand points as has been mentioned by Wright and Hall (1961):

(a) Humanitarian

(b) Technical efficiency

In modern surgical technique safe and satisfactory anesthesia is essential for both patient as well as for surgeon. Modern anesthetic practice is desired to meet three essential demands:

(a) The patient's safety and comfort.

(b) Facilitation of surgeons work

(c) Prompt return of the patient to a normal physiological state.

The goat belongs to the family Bovidae (hollow-horned ruminants) and is the member of the genus ***Capra.***

The earliest use of anesthetic agents dated back to 2250 BC as recorded on a Babylonian clay tablet. The introduction of general anesthesia for safe and painless surgery was established between 1842 and 1847 (Jones, 1974). Primarily Intravenous anesthesia was used by Ore in 1875 (cited by Lumb and Jones, 1996) but revolutionary changes occurred after the introduction of Barbiturates in late 1920s and 1930s (Clarke, 1938). Xylazine was synthesized in Germany in 1962 (Hall and Clark, 1991) and was the first α -2 adrenergic agonist to be used as a sedative and analgesic by veterinarians. Reports on the effectiveness of xylazine as an anesthetic adjunct began to appear in the 1970s, but it was not until 1981 that xylazine anesthetic action was linked to the stimulation of central α -2 adrenergic receptors (Clough and Hutton 1981; Hsu 1981). Ruminants are the most sensitive of the domestic animals to the action of xylazine (Goodman Gilman *et al.*2001). Ketamine is a unique general anesthetic first introduced into human medicine in 1965; in 1970 it was introduced for anesthesia in the cat (Goodman Gilman *et al.*2001). Since then many attempts have been made to use them in different forms and combinations.

There is no single anesthetic method or agent that produces ideal anesthesia under all circumstances. So there is a need for using combination of drugs or methods which can be safely used to produce the desired effect.

Keeping these aspects in view an attempt has been made to introduce xylazine and ketamine hydrochloride alone and in combination as general anesthetic along with diazepam as pre anesthetic in the practice of caprine anesthesia.

Diazepam, a member of Benzodiazepine group is known to have a synergistic interaction with α-2 agonist. Benzodiazepine can produce

sedation, hypnosis, decreased anxiety, muscle relaxation, anterograde amnesia and anticonvulsant activity, but the benzodiazepine do not produce a true general anesthesia since awareness usually persists and relaxation sufficient to allow surgery cannot be achieved (Goodman Gilman *et al.*2001). Diazepam reduces the dosage of general anesthetic (xylazine and ketamine), as well as induction and maintenance become safe. It has been found that in combination diazepam along with α -2 agonist viz. xylazine, medetomidine and romifidine proved to be good combinations for preanesthetic medication in goats (Chitale, 1998).

Benzodiazepines are not analgesics, nor can they produce a state of surgical anesthesia when used alone. It is thus necessary to combine several drugs to achieve surgical levels of anesthesia with a balance of sedation, analgesia, amnesia, relaxation and freedom from reflex stimulation (Goodman Gilman *et al.*2001).

Diazepam; a tranquilizer has calming, muscle relaxant, and anticonvulsant effect (Lumb and Jones, 1996). When a tranquilizer was given as a preanesthetic, induction of anesthesia was easier, the dose of anesthetics required was reduced, and recovery from anesthesia was usually smoother and free from struggling and vocalization.

Although Bovine and Caprine are unsuitable subjects for general anesthesia. However, in recent past caprine anesthesia has received more attention but the endeavours could not make much head way forwards obtaining satisfactory results (Kelawala and Parsania, 1992) and thus anesthesia is still a challenging problem for this species.

The present study was designed to study the effect of these combinations on physiological and biochemical parameters in goats.

So, it has become essential to evolve such type of anesthetic combination for surgical procedures in goats which are safe as well as effective and could replace the existing traditional method having associated risks.

The result of the present study would 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. The findings of this study would probably make anesthesia a much safer and comfortable experience to the clinician as well as the patient. Keeping in view the above mentioned facts, the present study has been undertaken with following objectives.

- To study the effect of Diazepam as preanesthetic along with α -2 agonist (Xylazine) as a general anesthetic in caprine.
- To study the effect of Diazepam as preanesthetic along with Ketamine as a general anesthetic in caprine.
- To study the effect of Diazepam as preanesthetic in combination with Xylazine and Ketamine as a general anesthetic in caprine.
- Comparative study of all the above combination as general anesthetic in caprine.

* * * * * * *

REVIEW OF LITERATURE

Available literatures reveal scanty information regarding use of diazepam as pre-anesthetic with xylazine and ketamine alone and in combination as general anesthetic in caprine, but Humphrey (1971), conducted extensive clinical trials with ketamine hydrochloride and observed it as safe and effective general anesthetic in canine surgery when it was used in dose rate of 20 mg/kg b.wt.

Strub (1971) studied optimal anesthetic dose of xylazine in sheep by I/M @ 0.3 mg/kg b.wt. The maximum effect was marked in 15 minutes and lasted up to 45 minutes after injection. Good results were obtained in 59 sheep anesthetized with the drug in which laparotomy and caesarian section were done. Some of the lambs born by caesarian 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 prolonged the duration of analgesia at low doses of anesthetic and provided sedation of sufficient duration to assure quite recovery.

Berlinger and Lakatos (1972) reported that ketamine hydrochloride was suitable for short, simple surgical operations at a dose rate of 20 mg/kg (I/M) in cats. Anesthesia was achieved after 3-4 minutes and lasts for about 20 minutes.

Hopkins (1972) observed that intramuscular administration of a small dose of xylazine produced sedation, analgesia and muscle relaxation in cattle. These characteristics of xylazine and absence of its serious side effects should make it a valuable agent of chemical restrain for cattle.

Thurmon *et al.* (1973) demonstrated that ketamine hydrochloride rapidly immobilized the patients when given I/V or I/M in sheep. 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 dosage used (22 to 44 mg/kg) were adequate for short surgical and diagnostic procedures. The recovery was smooth and rapid.

Oeppert (1973) reported that ketamine and xylazine either alone or in combination 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 had a cardiovascular stimulant effect and therefore a very safe anesthetic agent under various adverse situations.

Kumar *et al.* (1976) used xylazine in combination with ketamine and observed skeletal muscle relaxation and duration of analgesia in domestic goats during a variety of surgical procedures. Salivation was moderate in all goats.

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, leukocytes and hemoglobin concentration were reduced at maximal sedation; whereas ESR was marked increased. Neutrophilia with corresponding lymphocytopenia was also

observed. Increased blood glucose was also observed which lasted only for 48 hours.

Shokry *et al.* (1976) used xylazine at the dose rate of 0.1 and 0.3 mg/kg in sheep. They studied serum glutamic oxaloacetic transaminase, 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 hyperglycemia after xylazine administration.

Kumar and Singh (1978) reported the effect of xylazine @ 2.5 mg/kg (I/M) used in minor surgery under local procaine anesthesia 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 hemoglobin concentration and a slight increase in blood sugar at the time of maximum sedation in all the cases.

Campbell *et al.* (1979) observed the haemodynamic effects of sedative level doses of xylazine in five calves. They observed prolonged reductions in heart rate, cardiac output, and arterial blood pressure. In there opinion depressed myocardium resulted from xylazine administration and sedation by xylazine was 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).Plasma glucose values increased to 195 ± 15 mg/dl at15 minutes to 305 ± 10 mg/dl at 3 hrs .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) used ketamine and xylazine in combination 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 anesthesia 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 anesthesia. Transient changes in haemocytological and glucose level 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 anesthesia lasting for 40-45 minutes during which different surgical procedures were carried out. A slight reduction in respiration, heart rate and rectal temperature during surgical anesthesia were recorded. Recovery was smooth and uncomplicated. Transient changes in erythrocytes, leukocytes, and haematocrit, hemoglobin, Na, K, Cl and glucose values were compensated in 48 hours. The combination of xylazine and ketamine was found satisfactory in pediatrics 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.

They reported that ketamine stimulated the autonomic nervous system and produced tachycardia and increased blood pressure in goats. Xylazine suppressed the autonomic nervous system, hence, they 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 anesthesia in goats. Atropine was used to control excessive salivation.

Amer and Misk (1980) injected xylazine at the dose rate of 0.2 mg/kg body weight in six female goats and observed by an increase in glucose, urea nitrogen and cholesterol levels and a decrease in chloride when blood serum and cerebrospinal fluid were examined.

Knight (1980) reported that α–2 agonists like xylazine, detomidine and medetomidine are centrally acting, non narcotic analgesic with sedative, myorelaxant and local anesthetic 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. In their opinion both these effects might 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 concentrations 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 was significantly depressed for 30 minutes after xylazine administration.

Hsu (1981) used xylazine on mice and newly hatched chicken and observed it as central nervous system depressant. 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 the use of yohimbine as an antagonist.

Waterman (1981) observed that respiratory and pulse rates decreased after xylazine administration, but increased 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 was smooth in all the cases.

Muggaberg and Brockman (1982) observed a transient hyperglucagonaemia, hypoinsulinaemia and hyperglycemia 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 α – adrenoreceptors.

Samy *et al.* (1982) conducted experiments with mixture of ketamine (3 mg/kg) and xylazine (0.3 mg/kg) on sheep. Anesthetic effect was obtained in small doses. The average anesthetic period persisted for 75 minutes. Clinical studies revealed increase in respiratory rate as well as decrease in pulse rate and body temperature. Study of haemogram revealed decreased level of erythrocytes, hemoglobin 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 level of BUN was marked

elevated. The total serum protein, calcium and inorganic phosphorus showed slight changes. The blood parameters returned to their preanesthetic values within 48 hours after anesthetization.

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 either the pattern or frequency of respiration in animals receiving ketamine. In their opinion pulse rate did not increase to the level induced by ketamine alone in goats when combination of atropine, xylazine and ketamine were used. That was probably due to the parasympathomimetic action of xylazine.

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

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 mechanisms but it was probably related to other mechanisms which depressed CNS as well.

Islas *et al.* (1985) reported that epidural administration of ketamine in goat produced potent analgesia without respiratory depression, urinary retention, neurologic sign and discomfort.

Singh *et al.* (1985) in their evaluation of xylazine-ketamine anesthesia in buffaloes injected xylazine intramuscularly (0.22 mg/kg) followed 1-5 minutes later by ketamine intravenously (2mg/kg). This combination produced satisfactory anesthesia for 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.

Kumar *et al.* (1986) reported that ketamine; an 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. Temperature and respiration rate remained unaffected but the heart rate was significantly increased up to 30 min. after administration of ketamine which was declined to normal levels by 120 minutes.

Nolan *et al.* (1987) studied the antinociceptive activity of I/V administration of ∝-2 adrenoreceptors agonists. Clonidine and xylazine was measured in sheep using thermal and mechanical pressure threshold detection 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 ∝-2 adreno-ceptors.

Vicente *et al.* (1987) formulated anesthetic regimes of ketamine and xylazine i/m at doses of 5 mg and 0.2 mg (I), 10 mg and 0.2 mg (II) 10 mg and 0.3 (III) and 10 mg and 0.3 mg (IV) per kg of b.wt. in sheep. Rumenotomy was done after 24 hours of fasting and 12 hours 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 and 0.2 mg/kg.

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 (2.5mg/kg) I/M in domesticated camel. Either drug used separately was suitable for sedation and analgesia, but the mixture of xylazine and ketamine was superior to either drug 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 hyperglycemic effect might be due to an ∝-adrenergic inhibition of insulin released by stimulation of $\propto_2$-receptors in the pancreatic β-cells and to an increased glucose production in the liver in anaesthetized rats.

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

Skarda *et al.* (1989) elucidated that a dose dependent sedation has been observed in cow after caudal epidural administration of ∝-2

agonists (xylazine).They attributed that the sedative action of xylazine was due to its central ∝-2 adrenergic effects.

Vigo *et al.* (1989) observed good analgesia and rapid recovery with 1-2 mg/kg xylazine (I/M) as preanesthetic, which was followed by 10-18 mg/kg ketamine (I/M) 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 was unknown. Heart rate and respiratory rate were significantly decreased and the survival contractions were decreased markedly after the induction of anesthesia.

Le Blance *et al.* (1988) used xylazine epidurally which resulted in significant analgesia for various surgical procedures in the perineal region of horses. The duration of analgesia from single injection of 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 was concluded that prolonged regional analgesia produced by epidurally administration of xylazine in horses, were sufficient for clinical use.

Skarda *et al.* (1990) used 0.05 mg/kg of xylazine injected into the caudal epidural space in cattle which induced analgesia, marked sedation, ataxia and depression of respiratory, cardiovascular and ruminal motor function. They further elucidated that tolazoline when administered intravenously @ 0.3 mg/kg reversed most rumen hypo-motility and cardiopulmonary depression as well as undesirable pharmacologic effects of xylazine without significantly affecting analgesia and sedation.

Kelawala *et al.* (1991) conducted haematological and biochemical studies on ketamine, propofol and diazepam. They 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 anesthesia 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 up to 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 was 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 dose level of 0.3 mg/kg body weight, 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 dose regimens.

Pandey *et al.* (1991) studied the effect of Diazepam and Ketamine on canine. They reported that the diazepam (@ 3 mg/kg) and ketamine (10 mg/kg) have induced anesthetics effect for an average duration of 37.00 ± 3.29 minutes. During anesthesia experimental animals showed drop in pulse rate respiration rate and body temperature. There was

significant increase in total leukocyte count and neutrophils percentage, while lymphocytes were dropped significantly.

Kelawala and Parsania (1992) studied ketamine, propofol and combination of propofol and ketamine as general anesthetic in goats premeditated with diazepam. In the goats where ketamine was used as sole anesthetic agent there was significant rise in heart rate, respiratory rate and decrease in body temp. There changes were insignificant in animals when propofol was used alone. However, heart rate and respiratory rate was significantly increased but body temperature 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 than xylazine alone and of longer duration than either agent given alone.

Ameerjan *et al.* (1992) used diazepam and showed that diazepam eliminated muscular hyper-tonicity provided optimum anesthesia with good degree of analgesia at lower dosage of ketamine and assured a quiet and uneven full recovery.

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 and 0.07 mg/kg and lignocaine hydrochloride 0.05 mg/kg) given into first intercoccygeal space. It was concluded that xylazine produced prolonged analgesia and sedation with better maintenance of hind limb strength than lignocaine hydrochloride.

Chakarbarty and Das (1993) observed that xylazine; ketamine anesthesia was well tolerated by Siberian tiger and can be used safely in this species.

More *et al.* (1993) evaluated the efficacy of diazepam-xylazine-ketamine anesthesia on calves ageing in between 6-12 months. 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 anesthesia were evidenced. DCL revealed significant neutrophilia with corresponding lymphocytopenia in animals of group II only.

Raidurg and Ranganath (1994) demonstrated that xylazine @ 0.05 mg/kg was given epidurally in calves which 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 was concluded that xylazine @ 0.05 mg/kg was suitable for the use as an epidural analgesic in calves.

Ekka *et al.* (1996) used ketamine hydrochloride 12 mg/kg in atropinised 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.

Kumar *et al.* (1996) reported ∝ -2 agonist (Detomidine) can be used safely as preanesthetic with ketamine in goat. They observed that the duration of anesthesia and muscle relaxation were greater in animals given atropine - detomidine – ketamine as compared to the animals given atropine – xylazine – ketamine combination.

Pandey *et al.* (1996) studied the utility and safety of xylazine-ketamine combination with and without diazepam in horses. They reported that the induction of anesthesia 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 anesthesia 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 and ketamine caused 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) used ketamine and xylazine epidurally for hindquarter surgery in ruminants. They performed surgery on 35 clinical cases and reported the efficacy of epidural administration of ketamine at a dose rate of 2.5 mg/kg and xylazine at 0.05 mg/kg (18 goats, 16 cattle and one buffalo) and performed various surgery. 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 epidurally in lumbosacral space and observed good analgesia of hind quarter without any alarming clinical side effects. Ketamine in combination with xylazine produced a longer duration of anesthesia in comparison to ketamine or xylazine alone, which might be due to synergistic interaction between ketamine and xylazine.

Barbalia *et al.* (1998) conducted clinical and physiological studies on epidural use of lignocaine hydrochloride, ketamine and combination of lignocaine hydrochloride + 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; however it was compensated within 30 minutes after onset. Epidural injection of lignocaine in conjunction with ketamine was superior and can be used in routine clinical practice.

Chitale *et al.* (1998) observed the use of ketamine after Premedication with diazepam – xylazine (Gr. A), diazepam - medetomidine (Group 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 ∝ -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 ∝ -2 agonists caused 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 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 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 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 parameters.

Chitale *et al.* (1999) observed increased serum glucose level after administration of ketamine premeditated with ∝-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 ∝ -2 agonists including xylazine which ware employed as agents for the production of spinal anesthesia in different species of animals.

Pratap *et al.* (1999) used ketamine @ 3 mg/kg and ketamine @ 3 mg/kg along with xylazine @ 0.05 mg/kg 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 and motor inco-ordination were more pronounced and duration of analgesia was also more in group B. It was concluded by them 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 (@ 1 mg/kg) and ketamine + lorazepam (@ 0.2 mg/kg) on 6 goats in each group (I, II and III). Atropine sulphate (@ 0.05 mg/kg) was administered to all the 18 goats half an hour before anesthesia. 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.

Akhare *et al.* (2003) studied the biochemical effects of ketamine in goats premeditated with diazepam, haloperidol and acepromazine. None of these combinations used appeared to cause alarming changes in different biochemical parameters and may be considered safe for use in goats.

Kinjavdekar *et al.* (2005) conducted experiment to study the effect of spinally administered ketamine and its combination with xylazine or medetomidine in goats. The result showed that the combination of ketamine with Xylazine or Medetomidine produced comparable degree of transient cardio pulmonary and haemodynamic changes after their lumbosacral spinal administration in goats.

Sahay and Das (2005) evaluated propofol alone and with ketamine for anaesthesia in atropinised goats. They suggested that propofol could be employed alone safely in goats. Ketamine may be useful in combination with propofol to produce longer duration of surgical anaesthesia in goats.

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MATERIALS AND METHODS

The study was conducted on 18 clinically healthy non-descript she goats aging one to two and half years and weighing in between 12 to 30 Kg. All the animals were kept under similar environmental condition and diet as far as practicable in the Department of Surgery and Radiology. Deworming was done 15 days prior to the experimentation and clinical examinations were conducted at a weak interval during pre-experimental period to observe the state of health.

Grouping of Animals:

All the selected animals were randomly divided into three groups viz. A, B and C consisting of 6 animals in each group.

Table showing design of experiment

Group	No. of Animals	Drug used	Dose(mg/kg body weight)	Route of Administration
A	1	**Diazepam* +Xylazine****	**0.75 + 0.05**	**I/V + I/M**
	2	Do	Do	Do
	3	Do	Do	Do
	4	Do	Do	Do
	5	Do	Do	Do
	6	Do	Do	Do
B	7	**Diazepam + Ketamine*****	**0.75 + 5**	**I/V + I/M**
	8	Do	Do	Do
	9	Do	Do	Do
	10	Do	Do	Do
	11	Do	Do	Do
	12	Do	Do	Do
C	13	**Diazepam + Xylazine+Ketamine**	**0.75 + 0.05 + 5**	**I/V + I/M + I/M**
	14	Do	Do	Do
	15	Do	Do	Do
	16	Do	Do	Do
	17	Do	Do	Do
	18	Do	Do	Do

* Diazepam (**Calmpose**$^{(R)}$, 5mg/ml, Ranbaxy India Limited).

** Xylazine Hydrochloride (**Xylaxin**$^{(R)}$, 20mg/ml, Indian Immunological Limited).

***Ketamine Hydrochloride (**Ketajet-50**$^{(R)}$, 50mg/ml, Sterfil Laboratories Pvt. Limited).

Pre- Anesthetic Preparation of Animals:

Food and water were with held for 24 hours and 12 hours respectively before the start of the experiment.

The animal was weighed just before the administration of anesthetics. Temperature, pulse and respiration rate of the experimental animals were recorded and the region of the jugular vein was shaved. The site of administration was aseptically prepared before administration of drug. Required parameters ware recorded and blood samples were collected before administration of anaesthetic agents (0 hour) for different biochemical parameters.

Methods of Experimentation:

Each animal was medicated separately as mentioned in the design of experiment there after different clinical and anesthetic effects were observed blood samples were collected at 1 hour, 2 hours, 3 hours, and finally at 24 hours for the estimation of different biochemical parameters. Clinical and anesthetic parameters were recorded at the time interval of 5, 10, 15, 20, 30, 45, 60, 75, 90, 105 and 120 minutes after drug administration. Respiration rate, pulse rate, rectal temperature and colour of visible mucous membrane ware recorded before and after the induction of the anaesthetic agents as mentioned above.

The duration after which the stool and the urine ware voided and its frequency was also recorded after administration of anesthetic agents. The effect on salivation was also studied.

Anesthetic observations included period of induction, duration of anesthesia and recovery periods in all of the experimental animals. The effects of different reflexes like corneal, palpebral, pedal and cutaneous were marked. The extent and magnitude of analgesia was ascertained by pin-prick

Figure No. 1. Photograph showing collection of blood from the jugular vein of experimental goats of group-C

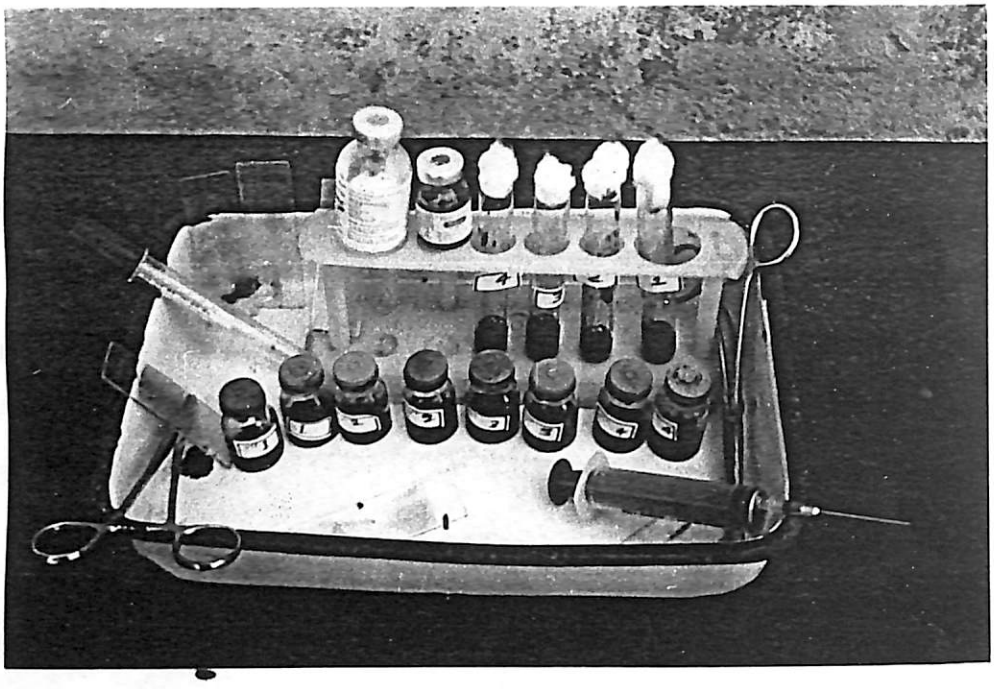

Figure No.2. Photograph revealing collected blood of different interval of time for biochemical estimation

response on body surfaces and the posture of animal which were recorded using 0 to 3 scale (**Table -1**) Sedation was examined by recording drowsiness and lowering of head.

Table 1

Scale	Degree of Analgesia	Reaction	Posture
0 -	No analgesia	Strong reaction to Pin-prick	Alert
1 -	Mild analgesia	Weak reaction to Pin-prick	Slight hand leg weakness
2 -	Moderate analgesia	Occasional reaction to pin-prick	standing with grat difficulty
3 -	Strong analgesia or Complete analgesia	No reaction to Pin-prick	Recumbent

Effect of drug on the region of limbs, tail, perineum, udder, thigh, digit, flank, thorax, ear and head were noted at different time intervals. Response to painful stimuli and pain threshold were assessed by pin-pricks, pinching by towel clamps or forceps. Period of induction, duration of anesthesia and recovery period were noted on the basis of physical symptoms and reflexes.

Biochemical parameters included evaluation of Serum Glucose, Serum Urea and Serum Creatinine.

For collection of blood serum 5 ml of blood was collected in each test tube without anticoagulant by sterile syringe from the jugular vein. The blood was allowed to clot within the tube in a slanting position for two hours then the serum was pipetted out in another test tube. The serum was

centrifuged at 3,500 rpm for 10 minutes. The supernatant serum was collected with a rubber bulb pipette. Then serum was analyzed for different biochemical parameters immediately. Serum glucose was estimated by Glucose-Oxidase (GOD) method (Frankel *et al.*1970), while Blood Urea Nitrogen (BUN) was estimated by Diacetyl Monoxime (DAM) method (Wootton, 1964) in order to investigate the kidney function before and after the administration of drugs and drug combination. Serum Creatinine estimation was done by Alkaline Picrate method. Statistical analysis was done by standard statistical methods as described by Snedecor and Cochran (1967).

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OBSERVATIONS AND RESULT

Rectal Temperature:

Rectal temperature was recorded in all the groups at different time interval from 0 to 120 minute. Mean with S.E*. of rectal temperature have been presented in **Table– 1**. Effects of administration of Diazepam, Xylazine and Ketamine alone and in combination on rectal temperature in all the groups were found to be non-significant ($P<0.05$). In group A and B, there was slight reduction in rectal temperature in the initial stage (5 to 20 minutes) but returned to the normal at the end of the experiment (120 minutes). In group-C, rectal temperature was static in comparison to group A and group B throughout the observation.

The analysis of variance did not reveal any significant ($P<0.05$) effects on rectal temperature up to the end of experiment (120th minute) due to different anesthetics **(Table-1B)**.

Pulse Rate:

Pulse rate of anaesthetized goats at different time interval from 0 to 120 minutes were recorded **(Table-2)**. After administration of Diazepam+Xylzine in group A, there was slight decrease in pulse rate which came normal at the end of the experiment (120^{th} minute).In group B, pulse rate increased after 10 minutes of administration of anaesthesia. A highly significant ($P<0.01$) increase could be seen between 10 to 60 minutes after medication and then it came to its normal range at the end of the experiment (120^{th} minute).

*- Standard Error

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
A	101.72 ± 0.26	101.32 ± 0.38	101.14 ± 0.46	101.12 ± 0.46	100.01 ± 0.50	100.00 ± 0.71	100.00 ± 0.71	100.20 ± 1.04	100.42 ± 1.12	101.20 ± 1.08	101.40 ± 0.97	101.68 ± 0.72
B	102.12 ± 0.20	102.10 ± 0.21	102.06 ± 0.20	102.08 ± 0.22	102.14 ± 0.22	102.10 ± 0.18	102.12 ± 0.20	102.10 ± 0.18	102.10 ± 0.16	101.08 ± 0.16	102.10 ± 0.14	101.80 ± 0.14
B	101.34 ± 0.34	101.34 ± 0.36	101.34 ± 0.36	101.36 ± 0.28	101.42 ± 0.30	101.33 ± 0.32	101.38 ± 0.28	101.42 ± 0.40	101.48 ± 0.48	101.52 ± 0.52	101.60 ± 0.64	101.96 ± 0.68

Means bearing no superscripts in each column are not differ significantly (P<0.05)

Table – I A

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

Group	Source of Variation	df	MS	F
Group A	Between periods	11	4.88	1.66 NS
	Error	60	2.94	
Group B	Between periods	11	0.06	0.18 NS
	Error	60	0.33	
Group C	Between periods	11	1.94	1.85 NS
	Error	60	1.05	

NS = (Non-significant)

Table – I B

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

Group	Source of Variation	df	MS	F
0 Min.	Between group	2	0.62	1.40^{NS}
	Error	15	0.44	
5 Min.	Between group	2	1.13	1.82^{NS}
	Error	15	0.62	
10 Min.	Between group	2	1.38	2.12^{NS}
	Error	15	0.65	
15 Min.	Between group	2	1.40	2.59^{NS}
	Error	15	0.54	
20 Min.	Between group	2	1.44	2.13^{NS}
	Error	15	0.67	
30 Min	Between group	2	2.98	2.73^{NS}
	Error	15	1.09	
45 Min.	Between group	2	3.27	2.61^{NS}
	Error	15	1.25	
60 Min.	Between group	2	7.57	2.74^{NS}
	Error	15	2.76	
75 Min.	Between group	2	12.42	2.78^{NS}
	Error	15	4.46	
90 Min.	Between group	2	7.32	2.52^{NS}
	Error	15	2.90	
105 Min.	Between group	2	8.12	2.13^{NS}
	Error	15	3.81	
120 Min.	Between group	2	6.24	2.31^{NS}
	Error	15	2.70	

NS = Non-Significant

Figure No.3. Photograph showing rectal temperature being taken from experimental goats of group – C

Figure No.4. Photograph showing auscultation of heart for recording its rate in goat of group- A

In group C, the experimental goats showed non-significant ($P<0.01$) variation throughout the experimental periods

In group C, the experimental goats showed non-significant ($P<0.01$) variation throughout the experimental periods.

Mean pulse rate in group A, B and C significantly ($P<0.01$) differ during experiment except from 0 to 5 minutes it was non-significant ($P<0.01$).

Pulse rate showed non-significant ($P<0.01$) differences between the groups at 5 minutes of experiment but at 15th minute pulse rate was 70$\pm$0.98, 77.8$\pm$0.82, 76.02$\pm$1.20 in group A, B and C respectively showing marked differences in between the groups. Group B animals showed great variation from 5th to 90th minutes of experiment, which was not seen in group A and C.

The analysis of variance revealed highly significant ($P<0.01$) difference in average pulse rate in each group at 0 to 120 minutes interval (**Table-2A**). At 0 minute the pulse rate was 75$\pm$ 0.74, 74.4$\pm$ 0.86, 74.8$\pm$1.08 in group A, B and C respectively but at 30th minute the average pulse rate was 64.00$\pm$0.78, 80.2$\pm$0.94 and 77.02$\pm$1.92 in group A, B and C respectively which indicated the pulse rate showed great variation in group B in comparisons to group A and C between 0 to 30 minutes.

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**
A	75.00^{Ad} ± 0.74	75.00^{Ad} ± 0.74	74.00^{Bd} ± 0.74	70.00^{Be} ± 0.98	68.00^{Ce} ± 0.66	64.00^{Be} ± 0.78	64.00^{Cef} ± 0.87	62.00^{Cf} ± 0.82	66.00^{Cf} ± 0.82	68.00^{Cf} ± 0.52	70.00^{Cefg} ± 0.44	72.00^{Bdg} ± 0.44
B	74.4^{Ad} ± 0.86	74.4^{Ad} ± 0.86	77.00^{Bd} ± 0.84	77.8^{Bd} ± 0.082	78.2^{Bd} ± 0.92	80.20^{Aef} ± 0.94	80.40^{Ae} ± 0.98	84.2^{Ae} ± 0.98	83.60^{Ae} ± 0.96	82.20^{Af} ± 0.82	78.20^{Afg} ± 0.81	75.40^{Adf} ± 0.84
C	74.8^{Ad} ± 1.08	75.00^{Ad} ± 1.06	74.6^{Ae} ± 1.08	76.02^{Ae} ±1.20	76.20^{Ae} ±1.80	77.02^{Ae} ±1.92	77.40^{Bd} ±2.02	76.02^{Bd} ± 2.02	75.08^{Bd} ± 1.54	74.06^{Bd} ± 1.12	74.2^{Bd} ± 1.08	74.2^{ABd} ± 0.98

A-C; Values bearing same superscript in a column did not differ significantly (P<0.01)
d-h; Values bearing same superscript in a row did not differ significantly (P<0.01)

Table – 2 A

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

Group	Source of Variation	df	MS	F
Group A	Between periods	11	72.04	27.87**
	Error	60	2.58	
Group B	Between periods	11	66.48	11.12**
	Error	60	5.97	
Group C	Between periods	11	51.02	5.64**
	Error	60	9.04	

** = Significant at (P<0.01)

Table – 2 B

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

Group	Source of Variation	df	MS	F
0 Min.	Between group	2	15.96	1.73^{NS}
	Error	15	9.21	
5 Min.	Between group	2	25.42	2.58^{NS}
	Error	15	9.85	
10 Min.	Between group	2	77.28	17.47^{NS}
	Error	15	4.42	
15 Min.	Between group	2	120.57	14.87^{**}
	Error	15	8.10	
20 Min.	Between group	2	156.27	14.38^{**}
	Error	15	10.86	
30 Min	Between group	2	134.54	13.56^{**}
	Error	15	9.92	
45 Min.	Between group	2	195.68	29.78^{**}
	Error	15	6.57	
60 Min.	Between group	2	272.40	38.27^{**}
	Error	15	7.11	
75 Min.	Between group	2	327.34	57.68^{**}
	Error	15	5.6	
90 Min.	Between group	2	218.46	67.83^{**}
	Error	15	3.22	
105 Min.	Between group	2	198.63	57.12^{**}
	Error	15	3.47	
120 Min.	Between group	2	196.07	67.08^{**}
	Error	15	2.92	

NS = Non-Significant

** = Significant ($P<0.01$)

Respiration rate:

Mean along with their S.E. of respiration rate of anaesthetized goats at 0 to 120 minutes time interval have been presented in **Table- 3.** Respiration rate at the start of the experiment was 19.60±0.42, 18.4±0.86 and 19.50±0.31 in group A, B and C respectively. Then respiration rate showed highly significant ($P<0.01$) variation from 5th to 120th minutes of experimentation. Respiration rate decreased after 5 minutes of experiment but returned to its normal level towards the end of the experiment (120th minute). In group B, respiration rate did not show any variation from 0 to 15th minute of experimentation, then rate of respiration increased to its peak (23.00 ± 0.62) at 60th minute after medication. There after the rate of respiration decreased till the end of the experiment (120th minute). After 60 minutes respiration rate did not show any significant ($P<0.01$) difference.

In group C, respiration rate was found highest in between 20 to 30 minutes of medication but there was non-significant ($P<0.01$) difference between 0 to 75 minutes of experiment. There was highly significant ($P<0.01$) difference between 75th minute to 90th minute of experimentation. From 90th minute to the end of the experiment (120th minute) respiration rate showed non-significant ($P<0.01$) variation

Analysis of variance (**Table -3B**) revealed a highly significant ($P<0.01$) difference in average respiration rate in between 5 to 120 minutes of experimentation among the groups.

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

Group	Period (minutes)											
	0	5	10	15	20	30	45	60	75	90	105	120
A	19.60^{Ad} ± 0.42	16.20^{Cg} ± 0.49	16.20^{Cg} ± 0.49	16.20^{BCg} ± 0.49	16.20^{BCg} ± 0.49	16.40^{Cfg} ± 0.47	17.20^{Cefg} ± 0.63	18.20^{Cdef} ± 0.45	18.20^{Cdef} ± 0.45	18.20^{Cdef} ± 0.45	19.00^{Bde} ± 0.58	19.20^{Bd} ± 0.44
B	18.40^{Af} ± 0.86	18.40^{Abf} ± 0.86	18.40^{Abf} ± 0.86	18.40^{Bf} ± 0.86	19.20^{Abef} ± 1.57	19.20^{Bef} ± 1.57	22.80^{ABd} ± 0.67	23.00^{Ad} ± 0.62	22.60^{Ad} ±0.28	22.60^{Ad} ± 0.33	21.60^{Ade} ± 0.33	21.60^{Ade} ± 0.33
C	19.50^{Af} ± 0.31	19.90^{Af} ± 0.64	20.10^{Aef} ± 0.39	20.60^{Aef} ± 0.46	23.00^{Ade} ± 0.24	23.00^{Ad} ± 0.19	22.80^{Ad} ± 0.19	22.60^{Abde} ± 0.15	22.40^{Abde} ± 0.26	22.00^{Bde} ± 0.19	22.00^{Bf} ± 0.19	22.20^{Bf} ± 0.16

A-C; Values bearing same superscript in a column did not differ significantly (P<0.01)
d-h; Values bearing same superscript in a row did not differ significantly (P<0.01)

Table – 3 A

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

Group	Source of Variation	df	MS	F
Group A	Between periods	11	12.25	7.24**
	Error	60	1.69	
Group B	Between periods	11	21.30	5.23**
	Error	60	4.07	
Group C	Between periods	11	6.24	9.14**
	Error	60	0.68	

** = Significant at (P<0.01)

Table – 3 B

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

Group	Source of Variation	df	MS	F
0 Min.	Between group	2	2.36	1.17^{NS}
	Error	15	2.01	
5 Min.	Between group	2	2.40	1.18^{NS}
	Error	15	2.06	
10 Min.	Between group	2	21.80	8.93^{NS}
	Error	15	2.44	
15 Min.	Between group	2	27.20	10.68^{**}
	Error	15	2.54	
20 Min.	Between group	2	35.20	7.20^{**}
	Error	15	4.88	
30 Min	Between group	2	42.13	8.34^{**}
	Error	15	5.05	
45 Min.	Between group	2	48.70	27.43^{**}
	Error	15	1.77	
60 Min.	Between group	2	35.04	26.40^{**}
	Error	15	1.32	
75 Min.	Between group	2	28.63	36.98^{**}
	Error	15	0.77	
90 Min.	Between group	2	26.20	38.14^{**}
	Error	15	0.68	
105 Min.	Between group	2	13.20	12.35^{**}
	Error	15	1.06	
120 Min.	Between group	2	11.13	14.36^{**}
	Error	15	0.77	

NS = Non-Significant **** = Significant at (P<0.01)**

Anaesthetic parameters:

Onset of action:

Mean along with their S.E. of onset of action (in minutes) of anaesthetized goats have been presented in **Table-4**. The average duration of onset of action were 2.52±0.03, 6.45±0.42 and 1.43±0.13 minutes in group A, B and C respectively .The onset of action was quicker in group C followed by group A and B. Group B animals showed longer duration of onset of action in comparison to group A animals.

Analysis of variance (**Table-4A**) revealed that there was highly significant ($P<0.01$) difference among the groups after induction of anaesthesia.

Duration of action:

Mean along with their S.E. of duration of action (in minutes) in anaesthetized goats in different experimental groups have been presented in **Table - 4**. The average duration of action were 74.00±3.49, 32.00±1.32 and 93.00±1.72 minutes in group A, B and C respectively. The duration of action was significantly longer in group C than group A and B; however, duration of action in group A was longer than group B. Analysis of variance (**Table - 4A**) showed highly significant ($P<0.01$) difference in duration of action in different groups.

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)
A	$2.52^{b} \pm 0.03$	$74.00^{b} \pm 3.49$	$92.00^{b} \pm 1.92$
B	$6.45^{a} \pm 0.42$	$43.00^{c} \pm 1.32$	$51.00^{c} \pm 1.32$
C	$1.43^{c} \pm 0.13$	$93.00^{a} \pm 1.72$	$121.00^{a} \pm 2.42$

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	df	MS	F
Onset of action	Between groups	2	16.32	61.34^{**}
	Within groups	15	0.26	
Duration of action	Between groups	2	3128.53	117.47^{**}
	Within groups	15	26.63	
Recovery period	Between groups	2	52.63	312.43^{**}
	Within groups	15	16.84	

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

Recovery period:

Mean along with their S.E. of recovery period (in minutes) in anaesthetized goats among different groups have been presented in **Table- 4**.The average recovery period was 92.00± 1.92, 51.00±1.32 and 121±2.42 minutes of group A, B and C respectively. Recovery in group C was longer than the group A and B. Recovery in group B (51.00±1.32) was quicker than group A (92.00±1.92).

Analysis of variance (**Table- 4A**) revealed highly significant ($P<0.01$) difference among the groups after induction of anaesthetic agents.

Analgesia:

Mean along with S.E on scale of analgesia for goats in different experimental groups have been presented in **Table-5**. Analgesia was recorded by using 0-3 scale to pin prick response.

In group A, analgesia was observed at 5th minute and lasted up to the end (120th minute) with maximum analgesia between 20th to 45th minute (2.00±0.00).

In group B, analgesia was recorded at 10th minute and persisted up to 45 minutes. The maximum analgesia (1.75±0.00) was marked at 20th minute. Animals of group B showed mild to moderate analgesia.

In group C, analgesia was recorded at 5th minute (1.95±0.00) and lasted up to the end of the experiment (120th minute).Analgesia was moderate to complete and lasted for longer duration. In group C, complete analgesia was detected between 20th to 45th minute of experimentation.

Table – 5

Showing Mean ± S.E. of scale of analgesia after administration of Diazepam, Xylazine, Ketamine and their combination.

Drug	Time Interval (minutes)											
	0	5	10	15	20	30	45	60	75	90	105	120
Diazepam + Xylazine	0.00 ± 0.00	0.50 ± 0.01	0.50 ± 0.01	1.63 ± 0.04	2.10 ± 0.00	2.10 ± 0.00	2.10 ± 0.00	1.90 ± 0.01	1.64 ± 0.01	1.20 ± 0.00	1.10 ± 0.00	1.00 ± 0.00
Diazepam + Ketamine	0.00 ± 0.00	0.00 ± 0.00	0.60 ± 0.03	1.45 ± 0.03	1.75 ± 0.00	1.50 ± 0.00	1.00 ± 0.01	0.00 ± 0.01	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
Diazepam + Xylazine + Ketamine	0.00 ± 0.00	1.95 ± 0.00	2.45 ± 0.01	2.95 ± 0.00	3.00 ± 0.00	3.00 ± 0.00	3.00 ± 0.00	2.85 ± 0.08	2.55 ± 0.02	2.00 ± 0.00	1.50 ± 0.00	1.00 ± 0.00

Sedation:

Mean along with S.E. on scale of sedation in anaesthetized goats in different group have been presented in Table – 6.

In group A, sedation started from 5th minute and continued up to 105th minute of experiment. Maximum sedation (2.80±0.02) was at 30th minute after medication. Sedation was mild to moderate in nature. In group B, sedation started from 5th minutes and lasted for 45th minute after medication. Sedation was mild and maximum sedation (2.00±0.00) was recorded at 20th minute.

In group C, sedation started from 5th minute which continued up to 105th minute. Complete sedation was recorded between 15th to 90th minute of experiment. Mild sedation was recorded at the end of the experiment which indicated that goats of group C were in complete sedation (3.00+0.00) during the experiment.

Reflexes:

Different reflexes after administration of anesthetics in different combination have been presented in **Table – 7**. In group A, the corneal reflex was present up to 5 minutes and at 10th minute reflex became sluggish but between 15th to 45th minute corneal reflexes was absent. At 60th minute experimental goats showed light reflex and it was detected till the end of experiment (120th minute). Palpebral reflex was sluggish at 10th minute and this reflex was absent between 15th to

Table – 6

Showing Mean ± S.E. of scale of sedation after administration of Diazepam, Xylazine, Ketamine and their combination.

	Time Interval (minutes)											
Drug	**0**	**5**	**10**	**15**	**20**	**30**	**45**	**60**	**75**	**90**	**105**	**120**
Diazepam + Xylazine	0.00 ± 0.00	1.95 ± 0.04	1.95 ± 0.04	2.45 ± 0.00	2.55 ± 0.00	2.85 ± 0.02	2.64 ± 0.02	2.32 ± 0.00	2.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00	0.00 ± 0.00
Diazepam + Ketamine	0.00 ± 0.00	0.85 ± 0.02	1.24 ± 0.18	1.80 ± 0.00	2.00 ± 0.00	1.50 ± 0.00	1.00 ± 0.01	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.50 ± 0.00	0.00 ± 0.00
Diazepam + 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	3.00 ± 0.00	3.00 ± 0.00	2.00 ± 0.00	1.50 ± 0.02

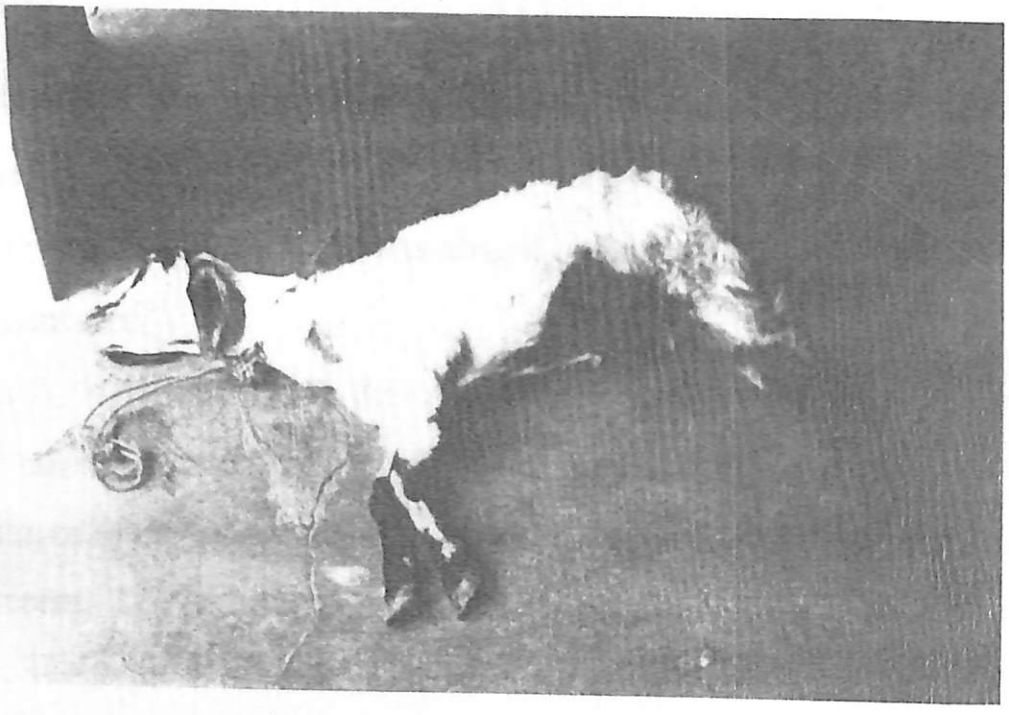

Figure No.5. Photograph revealing goat of group-A (Diazepam + Xylazine) goat in stage of surgical anaesthesia

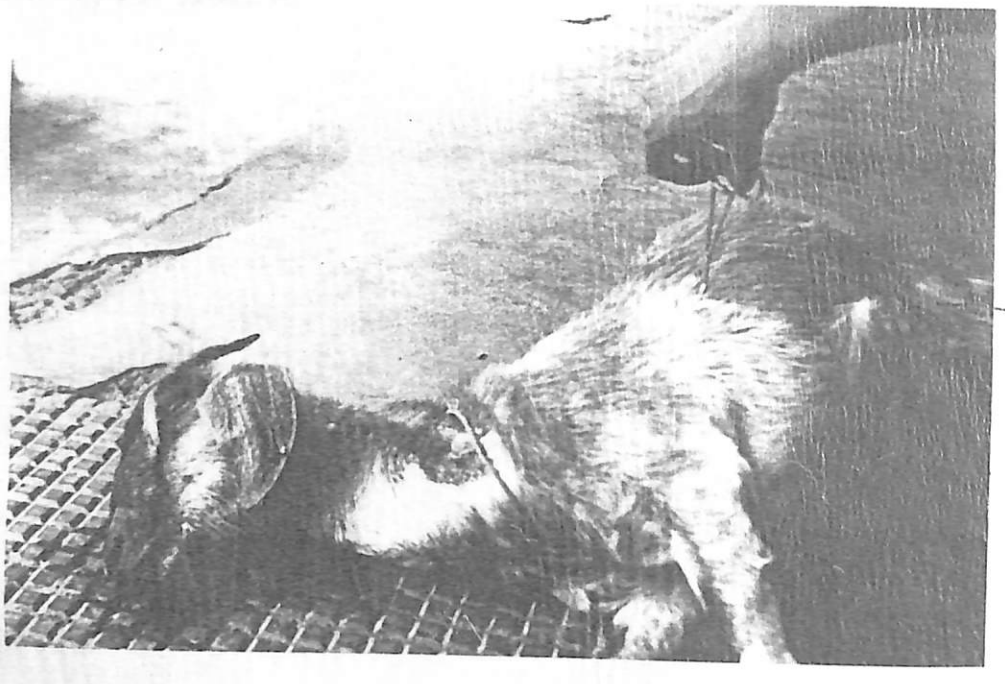

Figure No.6. Photograph showing recording of cutaneous reflex after induction of anaesthesia in group C

60th minute. Palpebral reflex reappeared after 75th minute of medication. Cutaneous reflex was absent between 10th to 75th minute of experimentation. Pedal reflex was absent between 10th to 60th minute of experimentation.

In group B, the corneal reflex was absent between 30th to 45th minute. The palpebral reflex was only sluggish between 20th to 45th minute of experiment and in the remaining period palpebral reflex was present. The cutaneous reflex was absent only during 15th to 30th minute. The pedal reflex was absent between 15th to 45th minute.

In group C, corneal reflex was present during whole of the experimental period. The palpebral reflex was also present throughout the experimental period (0th to 120th minute).The cutaneous reflex was absent between 5th to 105th minute. The pedal reflex was absent between 5th to 90th minute.

Table – 7

Showing the status of different reflexes after administration of Diazepam and Xylazine

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

Table – 7 A

Showing the status of different reflexes after administration of Diazepam and Ketamine

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

Table – 7 B

Showing the status of different reflexes after administration of Diazepam + Xylazine + Ketamine combination

Time interval (minutes)	Corneal reflex	Palpebral reflex	Cutaneous reflex	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	Absent	Absent
105	Present	Present	Absent	Light
120	Present	Present	Sluggish	Light

Biochemical Parameters:

Blood glucose:

Mean along with S.E. for blood glucose at 0 to 24 hours interval under the influence of anesthetics in goats have been presented in **Table- 8.** At the start of experiment (0 minute) the average blood glucose level was 47.32±1.18, 49.00±2.32 and 46.21±1.32 in group A, B and C respectively.

In group A, blood glucose level increased from 1st to 3rd hour of experiment but returned to its normal at 24th hour.

In group B, there was increase in blood glucose level from 1st to 3rd hour of experiment but returned to normal at 24th hour.

Animal of group C, showed maximum glucose concentration at 1st hour of experiment, and then returned to the normal at 24th hour.

Analysis of variance (**Table-8A**) indicates there was highly significant ($P<0.01$) variation in blood glucose concentration at 1st hour between the groups but there was non-significant ($P<0.01$) difference in blood glucose level between group A and group B at 1st hour of experiment. The average level of blood glucose in these three groups at 24th hour after induction of anesthetics were very closer to the base value at 0 hour and did not differ significantly($P<0.01$).

Table – 8

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

Period Hours

Group	0	1	2	3	24
A	$47.32^{z} \pm 1.18$	$61.37^{by} \pm 3.17$	$79.46^{x} \pm 2.81$	$75.10^{x} \pm 2.10$	$47.18^{z} \pm 0.52$
B	$49.00^{z} \pm 2.32$	$62.14^{by} \pm 1.32$	$78.14^{x} \pm 3.92$	$86.42^{x} \pm 4.12$	$49.32^{z} \pm 2.12$
C	$46.21^{z} \pm 1.32$	$84.01^{ax} \pm 2.43$	$72.14^{xy} \pm 2.13$	$65.23^{y} \pm 4.08$	$45.15^{z} \pm 1.13$

a – b : Values bearings same superscript in a column did not differ significantly.

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

Table – 8 A

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

Period	Source of Variation	df	MS	F
0 Hr.	Between group	2	18.23	1.18^{NS}
	Error	15	15.44	
1 Hr.	Between group	2	1123.46	35.68^{**}
	Error	15	31.48	
2 Hrs.	Between group	2	187.43	3.48^{NS}
	Error	15	53.85	
3 Hrs.	Between group	2	113.63	1.63^{NS}
	Error	15	69.71	
24 Hrs.	Between group	2	33.12	1.98^{NS}
	Error	15	16.72	

NS = Non-Significant

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

Table – 8 B

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

Group	Source of Variation	df	MS	F
Group A	Between periods	5	782.32	32.56**
	Error	24	24.02	
Group B	Between periods	5	844.46	17.36**
	Error	24	48.64	
Group C	Between periods	5	1830.12	47.23**
	Error	24	38.74	

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

Blood Urea Nitrogen:

Mean along with S.E. of Blood Urea Nitrogen at 0 to 24 hours interval under the influence of different anaesthetic agents in goats have been presented in **Table- 9**. The average level of blood urea nitrogen was 24.24±0.38, 24.43±0.12 and 24.12±0.47 in group A, B and C respectively at start of the experiment.

The analysis of variance (**Table- 9A**) did not reveal any significant ($P<0.01$) difference between groups at different periods of experiment after induction of anaesthesia.

The analysis of variance (**Table- 9B**) revealed highly significant ($P<0.01$) difference between groups at different periods of experiment of group A and significant ($P<0.05$) difference in group B .The average blood urea nitrogen at first hour of experiment was 27.12±0.12, 25.12±0.48 and 25.91±0.23 in group A, B and C.The analysis of variance (**Table-9B**) revealed nonsignificant ($P<0.01$) difference among the groups.

Serum Creatinine:

Mean along with their S.E. of serum creatinine at 0 to 24 hours interval under the influence of different anesthetics in goats have been presented in **Table- 10**. The average concentration of creatinine at 0 hour of experiment was 1.29±0.02, 1.33±0.05 and 1.49±0.05 of group A, B and C respectively.

Table – 9

Mean ± S.E. of Blood Urea Nitrogen (BUN) (mg%) of goats at different periods of interval Under the influence of anesthetic agents.

Period (Hours)

Group	0	1	2	3	24
A	$24.24^{z} \pm 0.38$	$27.12^{x} \pm 0.12$	$26.16^{xy} \pm 0.38$	$25.12^{yz} \pm 3.2$	$24.12^{z} \pm 0.12$
B	$24.48^{yz} \pm 0.12$	$25.12^{xy} \pm 0.48$	$25.98^{x} \pm 0.18$	$24.63^{xyz} \pm 0.26$	$23.63^{z} \pm 0.12$
C	24.12 ± 0.47	25.91 ± 0.23	24.12 ± 0.13	23.12 ± 0.73	23.02 ± 0.13

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

Table – 9 A

Analysis of variance for the effect of anaesthetic agents on Blood Urea Nitrogen (BUN) (mg %) in goats.

Period	Source of Variation	df	MS	F
0 Hr.	Between groups	2	0.32	1.23^{NS}
	Error	15	1.33	
1 Hr.	Between groups	2	2.87	4.12^{NS}
	Error	15	0.69	
2 Hrs.	Between groups	2	2.62	2.94^{NS}
	Error	15	0.89	
3 Hrs.	Between groups	2	802.12	3.42^{NS}
	Error	15	234.53	
24 Hrs.	Between groups	2	0.27	0.16^{NS}
	Error	15	1.68	

NS = Non-Significant

Table – 9 B

Analysis of variance for the effect of anaesthetic agents on Blood Urea Nitrogen (BUN) (mg %) in goats.

Group	Source of Variation	df	MS	F
Group A	Between Periods	5	6.82	5.34^{**}
	Error	24	1.27	
Group B	Between Periods	5	3.51	3.72^{*}
	Error	24	0.94	
Group C	Between Periods	5	5.02	2.41^{NS}
	Error	24	2.08	

NS = Non-Significant

* = Significant at (P< 0.05)

** = Significant at (P<0.01)

The analysis of variance (**Table-10A**) revealed highly significant ($P<0.01$) variation in all the three group at 1, 2 and 3 hour, while nonsignificant ($P<0.01$) difference was observed among different groups at 24 hours following the induction of anaesthetic agents. A significant ($P<0.01$) rise in the average level of creatinine was observed up to 3 hours. The analysis of variance (**Table-10B**) revealed nonsignificant difference in group A and significant difference in group B and highly significant ($P<0.01$) difference in group C.

The concentration of serum creatinine returned to the initial level at the end of 24^{th} hour as at the start of experimentation and did not differ significantly ($P<0.01$).

Table – 10

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

Period (Hours)

Group	0	1	2	3	24
A	1.29 ± 0.02	$1.42^{b} \pm 0.04$	$1.39^{b} \pm 0.03$	$1.35^{b} \pm 0.04$	1.30 ± 0.03
B	$1.33^{xy} \pm 0.05$	$1.43^{bx} \pm 0.06$	$1.43^{bx} \pm 0.05$	$1.40^{bx} \pm 0.06$	$1.19^{y} \pm 0.05$
C	$1.49^{y} \pm 0.05$	$1.75^{ax} \pm 0.04$	$1.85^{ax} \pm 0.06$	$1.83^{ax} \pm 0.06$	$1.38^{y} \pm 0.06$

a – b : Values bearings same superscript in a column did not differ significantly.

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

Table – 10 A

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

Period	Source of Variation	df	MS	F
0 Hr.	Between groups	2	0.05	3.27^{NS}
	Error	15	0.01	
1 Hr.	Between groups	2	0.19	16.9^{**}
	Error	15	0.01	
2 Hrs.	Between groups	2	0.29	31.27^{**}
	Error	15	0.01	
3 Hrs.	Between groups	2	0.32	30.13^{**}
	Error	15	0.01	
24 Hrs.	Between groups	2	0.05	4.02^{NS}
	Error	15	0.01	

** = Significant at ($P < 0.01$), NS = Non-significant

Table – 10 B

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

Group	Source of Variation	df	MS	F
Group A	Between Periods	5	0.017	2.21^{NS}
	Error	24	0.007	
Group B	Between Periods	5	0.047	2.89^{*}
	Error	24	0.016	
Group C	Between Periods	5	0.214	13.97^{**}
	Error	24	0.015	

NS = Non-significant

* = Significant at (P<0.05)

** = Significant at (P<0.01)

****

DISCUSSION

Physiological Observations:

Respiration rate:

The respiration rate significantly decreased in group A but increased in group B and C. In group B respiration rate was faster than that of group C.

Group A

The decrease in respiration rate started from 5th minute onward and remained till 90th minute and than a gradual increase was seen which came to normal level in 120 minutes of experiment. This decrease in respiration rate after Xylazine administration might be due to direct depression of respiratory center, similar findings were reported by Chitale *et al.* (1998), Kumar *et al.* (1976) and kinjavdekar (1998) in goats, Skarda *et al.* (1990), Rehage *et al.* (1994) and Kumar and Singh (1976) in cattle.

Group B

Respiration rate was observed significantly increased after administration of diazepam and ketamine. Respiration rate increased from 20 minutes onwards and remained increasing till 120 minutes of experiment. Respiration rate increased due to stimulation of respiratory centers by ketamine. Similar findings were also reported by Kumar *et al.* (1983), Islas *et al.* (1985) Chitale *et al.* (1998) in goats.

Group C

In initial stage a slight rise in respiration rate was observed after administration of Diazepam, Xylazine and Ketamine which gradually returned to the normal level at the end of experiment. Increased rate might be due to effect of Ketamine in the initial stage but decrease in respiratory rate in the later stage might be due to action of Xylazine. Similar finding

were also reported by Moens and Fregetton (1990) after administration of Ketamine and Xylazine in dogs, White *et al.* (1987) in domestic camel.

Rectal Temperature:

After administration of anesthetic agents in all the groups clinical observation revealed that they have slight or no effect on the body temperature. In group A, slight decrease in rectal temperature might be due to $\alpha - 2$ agonist which activate the hypothalamic α – receptors inhibiting the heat conserving mechanism. Similar observations were also reported by Kumar and Singh (1979) in bovine, Kumar *et al.* (1983) in goats. A significant reduction 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:

In all the groups after administration of anesthetic agents variation in pulse rate was observed.

Group A

A significant reduction in pulse rate was marked after 20 minutes of administration of the anesthetic agents; it might be due to central and peripheral suppression of sympathetic tone after administration of xylazine. Similar pattern of pulse rate was also reported by Fayed *et al.* (1989) in heifers and Varshney (1998) in ponies.

Group B

A significant rise in pulse rate was observed in this group. Pulse rate increased after 15 minutes of experiment till 90 minutes which came to its normal value at the end of the experiment. Increase in pulse rate was probably due to inhibitory effect of Ketamine on the parasympathetic

(Vagal) innervations of the heart and sympathomimetic effect on the heart. Increase in the release of catecholamine after Ketamine administration might also contributed to tachycardia.

Group C

Slight increase in pulse rate in the initial stage and its reduction towards the end of the observation period may be due to prolonged effect of $\alpha - 2$ agonist as compared to Ketamine. Similar findings were also reported by Pratap *et al.* (1998) in goats.

Anesthetic Parameter:

Clinical observations showed anesthesia and analgesia simultaneously among the experimental goats in each groups. Early onset of action was recorded in group C (Diazepam + Xylazine +Ketamine) followed by group A (Diazepam + Xylazine) and lastly in group B (Diazepam +Ketamine). Similar 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 Diazepam (0.75 mg/kg I/V) followed by Ketamine (5 mg/kg, I/M) produced a safe anesthesia. Auditory reflex was present. Muscular and other reflexes were observed through out the observation period.

Combination of Diazepam, Xylazine and Ketamine produced early onset of action. Xylazine depressed the CNS with sufficient muscular relaxation. Salivation was also scanty in comparision to Diazepam + Xylazine treated group. Animal easily attained the stage of surgical anesthesia, where any operation can be performed . Quick onset of action

was also reported by Pandey *et al.* (1996) in horse and Aithal *et al.* (1997) in goats.

Analgesia in group C was prolong as compared to group A and B. For prolong surgery Diazepam + Xylazine + Ketamine was suitable. It produced deep stage of anesthesia and good analgesia in goats. Similar observations were reported by Kumar and Singh (1979) in bovine calves, Singh *et al.* in buffaloes (1985). The recovery periods in the individual animal of all the groups were variable and there was a significant difference within the groups. Recovery was fast in group B animals followed by group A and prolong in group C. Prolong recovery period in group C might be due to synergetic action of diazepam, xylazine and ketamine causing more analgesia and anesthesia in this group and it caused delayed recovery. Similar finding was reported by Chitale *et al.* (1998) in goats. No mortality was detected in any group. Induction to recovery was soon and safe especially in group C, so margin of safety was wide when Diazepam, Xylazine and Ketamine were used in combination. Thus combination of these agents produced superior anesthesia and analgesia as compared to alone. Combination of anesthetic (group C) can be used in animals having poor physical health.

Salivation was scanty in group B and also in group C, but more salivation was seen in Diazepam + Xylazine treated group. This corroborated the findings of Ramaswamy *et al.* 1991 with Xylazine in dog.

Frequent urination was observed in most of the animal after administration of Diazepam + Xylazine or in combination with Ketamine during observation period. Urination was frequent in group A (Diazepam + Xylazine) but very less in group C (Diazepam + Xylazine + Ketamine). This might be due to inhibition of production and release of ADH.

Analgesia:

Analgesia was recorded by pin-prick method by response to pin-prick at ear, thorax, tail and digits using 0 – 3 scale. No analgesia, mild analgesia, moderate analgesia and complete analgesia were observed in all the groups. Duration of action was longer in group C followed by group A and group B this might be due to presence of Xylazine in group C and group A in combination with diazepam. Prolong analgesia might be due to stimulation of α – 2 adrenoreceptors in spinal cord and CNS thereby inhibiting the release of neurotransmitters and decreasing neuronal activity. In group B moderate, analgesia with shorter duration was observed. The synergistic action of Diazepam + Xylazine +Ketamine might be main factor which contribute towards excellent analgesia.

Sedation:

Sedation was observed after administration of anesthetic agents in group A, B and C. Mild to moderate sedation was observed within 5 minutes after administration of Diazepam + Xylazine and continued up to 70 minutes. In this period animal was tired showing drooping of head and eye lids with recumbency. Sedative action of Xylazine was due to stimulation of α-2 adrenoreptors which causes release of nor epinephrine or nor adrenaline in the central nervous system. The onset of sedation started together with the onset of analgesia after drug administration. Xylazine produced mild to moderate sedation after epidural administration in mare (Skarda and Muir, 1996) and goats (Aithal, *et al.* 1997)

After administration of Diazepam + Ketamine mild sedation was observed within 7-10 minutes and continued up to 60 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 development of systemic effects.

In group C, satisfactory and excellent sedation was noticed. Sedation was observed after 2-3 minutes of induction and it continued beyond 90 minutes. In this group animals remained in lateral recumbency from 5 minutes to 105 minutes. Excellent sedation produced in group C was due to central effect of Diazepam and Xylazine and potentiation by the Ketamine. The degree of sedation in group C (Diazepam + Xylazine + Ketamine) was greater in comparison to that produced by Diazepam + Xylazine or Diazepam + Ketamine. In group C, excellent analgesia of flank, abdomen and hind limb was observed.

Reflexes:

Different reflexes like corneal, palpebral and pedal were studied after administration of anesthetic agents. Absence of painful stimuli was noticed by lifting the tissue by Allis tissue forceps and for assessment of depth of anesthesia to pin-prick method. Depth of anesthesia was excellent in group C followed by group A and B. Reflexes was satisfactorily absent in group C as compared to group A and B.

Biochemical Studies:

Hyperglycaemia was observed in all the groups. Glucose level was higher in group C as compared to group A and B. In all the group glucose level was raised during 1 to 3 hours and came to normal within 24 hours. This observation was similar with the findings of Kumar and Singh (1976) in Cattle; Kumar and Singh (1978) in horses, Kumar and Thurmon (1979) in goat, Amer and Misk (1980) in goats, Peshin and Kumar (1983) in buffaloes, Fayed *et al.* (1989) in heifers, Kelawala *et al.* (1991), Singh *et al.*

(1999) in goats. Chitale *et al.* (1999) also observed hyperglycemia in goat after administration of Diazepam, Xylazine and Ketamine in combination as well as in alone.

Hyperglycemic effect might be due to α -adrenergic inhibition of insulin release from the pancreatic β-cell (Angel and Langer, 1988).

Blood Urea Nitrogen estimation showed fluctuation within the normal physiological level with slight rise at 1 and 2 hours in all the groups. Echner *et al.* (1979) in cattle and Amer and Misk (1980) in goats also reported similar observations.

A non-significant rise in Blood Urea Nitrogen was due to fasting of animals and depression of kidney function during use of anesthetic agents in goats. Similar observations also reported by Singh *et al.* (1999) in caprine and Singh *et al.* (1985) in buffaloes.

Serum creatinine level indicated a non-significant rise in all the three groups. These finding corroborated the observation of Hussain and Kumar (1988) in buffaloes, Singh *et al.* (1985) in buffaloes, Kelawala *et al.* (1991) in goat.

So, there was non-significant effect on serum creatinine level after administration of these anesthetic agent used alone or in combination.

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SUMMARY AND CONCLUSIONS

Use of xylazine and ketamine were evaluated in different combinations as general anesthetic after preanesthetic medication with diazepam in 18 clinically healthy she goats ageing in between 1 – 2.5 years and weighing in between 12 to 30 kg . The animals were randomly divided into 3 groups having six animals in each group.

Diazepam, Xylazine and Ketamine were injected at a dose rate of 0.75 mg / kg (I/V), 0.05 mg / kg (I/M), and 5 mg / Kg (I/M) respectively.

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; duration of sedation, extent and magnitude of analgesia. Sedation was judged by observing drowsiness, lowering of head and its posture.

Biochemical evaluation included estimation of serum glucose, blood urea nitrogen and serum creatinine. These observations suggested that all the above anesthetics can be safely used in caprine but the best result can be achieved when they are used in combination. There was lack of any post anesthetic complications or death. The following results were obtained:

- Xylazine when combined with diazepam produces deep sedation and optimum muscle relaxation in goats.
- Ketamine when combined with diazepam produces optimum sedation and analgesia for a shorter duration (25-40 minutes) but inadequate relaxation of muscle in goats.
- When combinations of all these three anesthetic agents were used there was an excellent analgesia, deep sedation, adequate

muscle relaxation for major surgical work and abolition of cutaneous reflexes permitting surgery.

- These anesthetic agents do not produce any significant biochemical alteration especially when used in combination.

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

- Diazepam, a benzodiazepam compound produced sedation hypnosis, decreased anxiety, muscle relaxation and anticonvulsion but the diazepam do not cause a true general anesthesia, since awareness usually persists and muscle relaxation is not sufficient to perform surgery.
- Xylazine when combined with diazepam as preanesthetic is efficient for any surgical intervention but anaesthetic effect last for 40-50 minutes.
- When diazepam combined with ketamine is suitable for minor surgery that can be perform for 15-20 minutes.
- Diazepam along with combination of xylazine and ketamine are suitable for performing any type of surgery which can be performed for 2 hours with good muscle relaxation along with eradication of complications which may go up to cardiac arrest.

The result of the present study may be elaborated by conducting more experiments on the animals and its clinical use wherever needed. The anaesthetics which have been used in present study can be used clinically by field veterinarians during their clinical practice.

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