ICAR AD HOC RESEARCH PROJECT ON

SEDATIVE, CLINICO-BIOCHEMICAL AND CARDIOPULMONARY EFFECTS OF PREANAESTHETICS AND GENERAL ANAESTHETICS IN NEONATAL CALVES

FINAL REPORT

(1/10/1999 – 30/09/2002)

Principal Investigator: ***Dr. SK Sharma***
Associate Professor

Co – Investigator: ***Dr. AC Varshney***
Professor & Head

Dept. of Veterinary Surgery & Radiology
College of Veterinary and Animal Sciences
CSK Himachal Pradesh Krishi Vishvavidyalaya
Palampur (HP) 176 062

ANNEXURE V

ICAR AD HOC RESEARCH PROJECT

FINAL REPORT (1/10/1999 – 30/09/2002)

1. Project Title:	**Sedative, clinico-biochemical and cardiopulmonary effects of preanaesthetics and general anaesthetics in neonatal calves**
2. Sanction No.:	1-20/97-ASR-IV dated 26.03.1999 / 13.04.1999
3. Date of start:	1/10/1999
4. Date of termination:	30/09/2002
5. Institution name:	Himachal Pradesh Krishi Vishvavidyalaya
Place:	Palampur
District:	Kangra
State:	Himachal Pradesh
Dept./Div. Name:	College of Veterinary and Animal Sciences
Actual location:	Dept. of Veterinary Surgery & Radiology
6. Principal investigator	
Name:	Dr. S.K. Sharma
Designation:	Associate Professor
Div./section:	Dept. of Veterinary Surgery & Radiology
Experience:	19 years and 7 months
Address:	Associate Professor Dept. of Veterinary Surgery & Radiology College of Veterinary and Animal Sciences CSK Himachal Pradesh Krishi Vishvavidyalaya Palampur (HP) 176 062

7. Co – investigator

Name:	Dr. A.C. Varshney
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8. Objectives:

Alleviation of pain is the primary and mandatory requisite in the conduct of any operative maneuver especially in the young bovine neonates. Anatomical and physiological considerations in the young one of any species do warrant institution and adoption of a very careful anaesthetic management so that the emergent is safe and uncomplicated. Maturation in the very young patients or neonates significantly modifies their response to anaesthesia since these subjects are comparatively more sensitive to the toxic effects of various drugs vis-à-vis adults. Many factors attribute to such response like under developed blood brain barrier, liver and excretory system in neonates.

Bovines form an integral part of dairy industry in our country. Bovine neonates do suffer from many congenital anomalies like atresia ani, knuckling, arthrogryposis, eye ailments etc. apart form parturition related problems like fracture, dislocation etc. Thus to undertake surgery in this delicate animal, anaesthetic technique should be adequately safe. Though some of such surgical maneuvers can be undertaken using local anaesthetic techniques, but this puts the patient under great stress because of its position, restraining method etc. Moreover neonate bovines are as good as monogastric animals; therefore general anaesthetic technique can safely be adopted in such patients' vis-à-vis adult ruminants. There are limited reports on neonatal anaesthesia in bovines. Therefore the project will be undertaken with the following objectives.

A) To evaluate certain commonly available anaesthetics for sedation in neonatal calves.

B) To study the clinico- biochemical effects of these anaesthetics in neonatal calves.

C) To evaluate the cardio-pulmonary effects of these anaesthetics in neonatal calves.

D) To evaluate the suitability of safe anaesthetic techniques/ combination for clinical use in neonatal calves.

9. Duration of the scheme: 3 years

10. Total cost of the scheme: Rs. 10, 75,840/-

Recurring: Rs. 2, 40, 000/-

Pay of officers: Rs. 3, 74,400/-

Year: 1/10/1999 to 30/09/2002

Name of the post	**Pay scale**	**Number of posts**	**Total**
Junior Research Fellows	Rs. 5000/- pm for I & II year and Rs. 5600/- pm for third year	Two	Rs. 3,74,400/-

Total

Year	Pay of officers	Pay of establishment (institutional charges)	TA	Other allow.	PF	**Contingencies** Recurring	Non Recurr.	Total
Ist year	1,20,000	20,000	---	-----	---	80,000	4,00,000	6,20,000
2nd year	1,20,000	20,000	---	-----	---	80,000	--------	2,20,000
3rd year	1,34,400	21,440	---	-----	---	80,000	--------	2,35,840

Non – recurring: Rs. 4, 00,000/-

Year	Recurring	Non recurring	Total
Ist year	80,000	4,00,000	4,80,000
2nd year	80,000	-------	80,000
3rd year	80,000	-------	80,000

TECHNICAL PERSONNELS EMPLOYED:

SNo.	Name and Designation	Date of joining	Date of leaving
1.	Dr. Rakesh Sharma	1/10/1999	28/08/2000
2.	Dr. Shakuntla	1/10/1999	23/04/2000
3.	Dr. Virender Pathak	27/06/2000	31/08/2000
4.	Dr. Paramasivan	25/10/2000	18/03/2001
5.	Dr. Mandeep Singh	12/02/2001	28/07/2001
6.	Dr. (Ms) Bindu Mahajan	14/08/2001	30/09/2001
7.	Dr. (Ms) Rinku Sharma	14/08/2001	16/01/2002
8.	Dr. Amit Mahajan	11/01/2002	31/03/2002
9.	Dr. Munish Gupta	5/02/2002	6/09/2002
10.	Dr. Jagmohan Singh	10/05/2002	30/09/2002

11. Total amount sanctioned: Nil
(in case of extension)

12. Total amount spent (in rupees): (**w.e.f. 1/10/1999 to 30/09/2002**)

Head	1/10/1999-30/9/2000	1/10/2000-30/9/2001	1/10/2001-30/9/2002	Total
Recurring	77833	37166	124204*	239203
Non recurring	269678	130172	-	399850
Institutional charges	-	20,000*	41440*	61440
Salary of research fellows	99016	54223	100102	253341
Total	446527	241561	265746	953834

*Some payments of year 1999-2000/2000-2001 were made in the year 2001-2002.

13. Results of Practical/Scientific value:

Based on the results of the ad hoc research project the following preanaesthetics/sedatives/surgical anaesthetic combinations can be used for premedication/achieving balanced surgical anaesthesia in the neonatal calves:

Sr. No.	Name of the preanaesthetics/sedative/tranquillizer/ Surgical anaesthetic combination	Dose rate	Route of administration	Type of effect
1.	Atropine sulfate	0.04 mg/kg	Subcutaneously	Anticholinergic
2.	Xylazine hydrochloride	0.22 mg/kg	Intramuscularly	Sedation
3.	Diazepam	0.3 mg/kg	Intravenously	Tranquillization
4.	Triflupromazine hydrochloride	0.5 mg/kg	Intravenously	Tranquillization
5.	Acepromazine maleate	0.75 mg/kg	Intravenously	Tranquillization
6.	Detomidine hydrochloride	0.02 mg/kg	Intramuscularly	Sedation
7.	Chloral hydrate, 4% solution	7.5 gm/100 kg	Intravenously	Narcosis
8.	Chloral hydrate +magnesium sulfate (Chloral-mag), 1:1, 6% solution	10 gm/100 kg	Intravenously	Narcosis
9.	Chloral hydrate +magnesium sulfate (Chloral-mag), 1:1, 6% solution 10 min later, Thiopentone sodium, 5%	10 gm/100 kg 15 mg/kg 'To effect'	Intravenously Intravenously	General anaesthesia
10.	Xylazine hydrochloride plus Ketamine hydrochloride	0.22 mg/kg | single 5 mg/kg | syringe	Intramuscularly	Balanced surgical anaesthesia
11.	Detomidine hydrochloride plus Ketamine hydrochloride	0.02 mg/kg | single 7.5 mg/kg | syringe	Intramuscularly	Balanced surgical anaesthesia
12.	Medetomidine hydrochloride	0.01 mg/kg	Intramuscularly	Sedation
13.	Atropine sulfate 10 min later, Medetomidine hydrochloride plus Ketamine hydrochloride	0.04 mg/kg 0.015 mg/kg | single syringe 10 mg/kg	Subcutaneously Intramuscularly	Balanced surgical anaesthesia
14.	Atropine sulfate plus Diazepam 10 min later, Thiopentone sodium 5%	0.04 mg/kg 0.3 mg/kg 15 mg/kg 'To effect'	Subcutaneously Intravenously Intravenously	General anaesthesia

Note:

1. The effects following Atropine sulfate or Acepromazine maleate administration were quite variable.
2. Out of the above-mentioned preanaesthetics/sedative/tranquillizer, Detomidine hydrochloride (@ 0.02 mg/kg, I/M), xylazine hydrochloride (@ 0.22 mg/kg, I/M), Diazepam (@ 0.3 mg/kg, I/V) and Medetomidine hydrochloride (@ 0.01 mg/kg, I/M) proved as best pre-anaesthetics (sedatives/tranquillizer) for the neonatal calves.

3. The combinations of Chloral hydrate-magnesium sulfate-thiopentone and Atropine-diazepam-thiopentone did produce general anaesthesia in bovine neonate calves but their use in clinical cases for balanced surgical anaesthesia is questionable due to prolong recovery time.
4. Xylazine + ketamine, Detomidine + ketamine and Atropine + medetomidine + ketamine combinations produced excellent and balanced surgical anaesthesia in neonate calves and are recommended for safe clinical use by the veterinarians in neonate calves as has been used in various clinical cases presented in the Teaching Veterinary Clinical Complex, College of Veterinary & Animal Sciences, Palampur (HP). (See Annexure-I)

14**. Papers published:**

1. S.K. Sharma, S.S. Mishra and A.C. Varshney. 1998. Evaluation of chloral hydrate anaesthesia in neonatal calves. Indian Vet. Med. J. 22: 69-72.
2. S.K. Sharma, S.S. Mishra and J.M. Nigam. 1998. Clinico-biochemical and electrocardiographic studies following xylazine-ketamine anaesthesia in neonatal calves. Proceedings 2nd Commonwealth Veterinary Conference, Feb. 22-27, 1998. Vol. II: 1125-1129.

Manuscript Submitted/completed:

1. Shakuntla. (2000). Evaluation of detomidine as sedative to ketamine anaesthesia in neonatal calves. M.V.Sc. Thesis. CSK HP Agril. University, Palampur (HP).
2. AK Singh. (2002). Atropine-medetomidine-ketamine as balanced anaesthesia for neonatal calves. M.V.Sc. Thesis. CSK HP Agril. University, Palampur (HP).
3. Pradeep Singh. (2002). Evaluation of diazepam-thiopentone anaesthesia in neonatal calves. M.V.Sc. Thesis. CSK HP Agril. University, Palampur (HP).
4. Jagmohan Singh. (2002). Evaluation of medetomidine hydrochloride as sedative in neonatal calves. M.V.Sc. Thesis. CSK HP Agril. University, Palampur (HP).

Papers presented at scientific meetings:

The following research articles have been presented in different scientific meetings/conferences at National and International levels.

1. Analgo-sedative and biochemical effects of xylazine and detomidine in neonatal calves. **(7th World Congress of Veterinary Anaesthesia, Berne, Switzerland, w.e.f September 20 – 23, 2000.)**
2. Clinico-sedative, cardiovascular and electroencephalographic studies following detomidine-ketamine anaesthesia in neonatal calves. **(25th Annual Congress of Indian Soc. Vety. Surgery held at CCS HAU, Hisar (Haryana) w.e.f. Dec. 5-7, 2001).**
3. Sedative and clinico-haematological effects of diazepam or triflupromazine in neonatal calves. **(25th Annual Congress of Indian Soc. Vety. Surgery held at CCS HAU, Hisar (Haryana) w.e.f. Dec. 5-7, 2001).**
4. Atropine-medetomidine-ketamine as a balanced anaesthetic technique for neonatal calves: clinico-sedative, cardiovascular and electroencephalographic studies. **(26th Annual Congress of Indian Soc. Vety. Surgery to be held at Veterinary College, Mumbai w.e.f Nov. 9-11, 2002).**

AWARDS CONFERRED ON THE RESEARCH OF THE PROJECT:

1. **Dr. NL Dutt Gold Medal, 2001** for 'Best paper presentation, Poster session' in 25th Annual Congress of Indian Soc. Vety. Surgery held at CCS HAU, Hisar (Haryana) w.e.f. Dec. 5-7, 2001. (Title: Clinico-sedative, cardiovascular and electroencephalographic studies following detomidine-ketamine anaesthesia in neonatal calves).
2. **'Best Research Paper Award, 2002 (Anaesthesiology session)** in 26th Annual Congress of Indian Soc. Vety. Surgery held at Veterinary College, Mumbai w.e.f Nov. 9-11, 2002. (Title: Atropine-medetomidine-ketamine as a balanced anaesthetic technique for neonatal calves: clinico-sedative, cardiovascular and electroencephalographic studies).

Manuscript under preparation: Nil

15. Detailed Progress Report:

a) The equipments listed in the project were purchased.

b) The following research work was carried out during the period under report:

During the period under report various sedatives/narcotics/anaesthetics were evaluated in 137 neonatal calves, 10-15 days old and weighing between 17-27 kg. All the animals were kept under same managemental conditions and were fed on milk. Water and milk were withheld for 3 to 6 hrs prior to the experimentation work and each animal was weighed on the day of experiment. **The necessary permission to carryout these experiments has already been granted by Institutional Animal Ethics Committee**. The detailed report of the results achieved is as under:

A) <u>EVALUATION OF ATROPINE SULFATE:</u>

Atropine sulfate @ 0.04 mg/kg, S/C, was used in 4 male neonatal calves during pilot trials. Its administration produced severe drying of muzzle and buccal cavity along with polydypsia. The heart rate was not affected. Since this drug was not producing the desirable effects in the neonatal calves and there was severe drying, it was not used along with sedatives, evaluated during the period of report.

B) <u>EVALUATION OF XYLAZINE:</u>

The evaluation of xylazine was carried out in 8 male neonatal calves, 10-15 days old and weighing 17-28 kg. Three animals were used for pilot trials using dose rates of 0.15, 0.20 and 0.22 mg/kg I/M, separately, to compute the dose of the drug. On subjective analysis a dose of 0.22 mg/kg body weight, I/M, was standardized in the neonatal calves for detailed evaluation in the remaining 5 animals.

a) Sedative and Clinical Studies:

Following drug administration the effect was seen within 1-3 min. The peak effect with complete analgesia remained for 20-30 min. However, deep sedation remained for 40-57 min. In one animal, analgesia was not observed. After completion of experiments, the animals were able to stand but with ataxia.

Xylazine administration resulted in mild to moderate depression of palpebral and corneal reflexes in neonatal cow calves, seen up to 45 minutes. In one animal mild depression was seen up to 60 minutes. Generally mild to moderate relaxation of neck and jaws was observed. However there was complete relaxation of neck and jaws between 5 and 45 minutes in three animals. The relaxation of tail and anal sphincter was mild following xylazine administration in cow calves. In all calves, swallowing reflex was abolished between 5 and 45 minutes after the drug administration. Analgesia of neck and trunk area was observed from 15 min interval till 45 minutes. But interdigital pin pricks revealed only mild to moderate analgesia. Normally xylazine administration did not cause any salivation or lacrimation except in one calf where mild to moderate lacrimation was observed at 5 and 15-minute interval.

A significant (P<0.05) to highly significant (P<0.01) decrease in rectal temperature and heart rate was observed in neonatal cow calves following xylazine administration (Table 1).

Table 1: Effect of xylazine anaesthesia on clinical and haematological parameters in neonatal cow calves (n=5, Mean±S.E)

Parameters	Base 0 min	Minutes after anaesthesia				
		5	15	30	45	60
Rectal temp. (^{o}C)	39.30 ±0.17	39.28 ±0.45	39.06 ±0.09	38.92** ±0.17	38.94* ±0.22	38.44** ±0.27
Heart Rate Per min	95.20 ±6.44	67.20** ±5.35	74.40* ±3.37	72.00* ±4.70	71.20** ±5.44	74.00** ±6.88
Resp. Rate Per min	22.40 ±1.46	45.00 ±12.32	41.40 ±6.83	26.80 ±2.73	20.60 ±3.17	20.20 ±3.15
Haemoglobin (g.%)	8.80 ±0.60	ND	8.28 ±0.59	8.20 ±0.64	8.24 ±0.59	8.12 ±0.67
PCV (%)	32.60 ±3.56	ND	32.00 ±3.41	31.40 ±3.38	30.80 ±3.08	31.20 ±3.55

*P<0.05; **P<0.01; ND = Not done

Maximum decrease in heart rate was observed at 5 min interval. There was an increase in respiratory rate at 5 and 15 minute interval but this increase was non significant (Table.1). At 30, 45 and 60 min intervals, respiratory rate remained within normal range.

b) Haematological Studies:

No significant changes were observed in haemoglobin and packed cell volume values of neonatal cow calves following xylazine administration (Table 1) when the values were compared to 0 hour (base) values.

c) Biochemical Studies:

The biochemical effects of xylazine administration in neonatal calves are presented in Table 2.

Table 2: Effect of xylazine anaesthesia on plasma biochemical parameters in neonatal cow calves (n=5, Mean±S.E):

Parameter	Base O min	Time interval after drug administration (min)			
		15	30	45	60
Glucose (mg/dl)	73.40 ±3.60	139.00* ±15.95	179.20** ±17.13	198.80** ±17.45	200.40** ±16.65
BUN (mg/dl)	15.20 ±1.56	14.20 ±1.43	15.00 ±1.70	14.00 ±1.44	15.60 ±1.99
Total proteins	6.24 ±0.26	6.20 ±0.24	6.06 ±0.31	6.02 ±0.32	5.70 ±0.23
Creatinine (mg/dl)	1.32 ±0.10	1.36 ±0.10	1.26 ±0.12	1.36 ±0.18	1.30 ±0.11
ALT (U/L)	10.00 ±0.94	8.60 ±1.45	6.00* ±0.75	8.60 ±0.36	7.20 ±1.11
AST (U/L)	31.00 ±3.53	27.60 ±3.95	25.60 ±3.88	29.20 ±3.19	28.40 ±4.09
Sodium (mEq/L)	122.40 ±3.32	124.00 ±3.88	126.40 ±1.43	124.00 ±1.79	126.00 ±2.59
Potassium (mEq/L)	4.32 ±0.15	3.88* ±0.08	3.98 ±0.11	3.94 ±0.12	4.10 ±0.10
Chloride (mEq/L)	98.46 ±1.14	97.38 ±1.25	99.56 ±0.40	99.12 ±0.73	99.10 ±1.11
LDH (U/L)	737.80 ±112.03	746.00 113.80	631.40 ±115.24	648.40 ±105.17	577.60 ±78.85

*P<0.05 **P<0.01

Initially xylazine caused a significant (P<0.05) increase in plasma glucose levels. Thereafter hyperglycaemia became highly significant (P<0.01) at 30, 45 and 60 min intervals. There was an evidence of hypokalaemia and this decrease in plasma potassium concentration was significant at 5 min interval. A significant decrease in ALT level was observed at 30 minutes. In this group, a non-significant

decrease in LDH concentration was also noticed. No significant variations were observed in other electrolytes (sodium and chloride), AST, blood urea nitrogen, creatinine and total proteins following xylazine administration in neonatal cow calves.

C) EVALUATION OF DIAZEPAM:

Diazepam was used in 8 male neonatal calves, 12-15 days old and weighing between 14-26 kg. Three animals were used for pilot trials and three dose rates (0.2, 0.3 and 0.5 mg/kg body weight, I/V) were used. On subjective analysis, depending upon the sedation produced, the dose rate of 0.3 mg/kg I/V was standardized for neonatal calves and the same was used in remaining 5 neonatal calves to evaluate sedative, clinical, haematological and biochemical parameters.

a) Sedative and Clinical Studies:

The onset of sedation was observed immediately following diazepam administration. The down time recorded was 1 min (sternal) in one animal and immediate to 2 min (lateral) in 3 animals whereas one animal remained standing throughout the period of sedation. The recovery time recorded was 19.3 ± 6.74 min (sternal), 42.0 ± 4.5 min (standing but ataxic) and 84.6 ± 12.4 min (normal gait), respectively. There was mild to moderate relaxation of neck, tail, and jaws up to 45 minutes of study where as mild to complete relaxation of anal sphincter was noticed throughout the period of study (up to 75 min). The depression of palpebral and photopupillary reflexes was moderate to complete, noticed up to 30 min interval only. Typical head resting on flank or ground was noticed during sedation with a sleepy look. Salivation or lacrimation was not observed. Drying of muzzle was noticed immediately after drug administration. During recovery period the animals were licking the muzzle and nearby objects. Shivering during recovery was noticed only in one animal in which there was 3^{o}F fall in rectal temperature. There was no analgesia. All the animals made violent efforts to stand during the sedation. The peak effect was noticed for 7-35 min with sedation remaining for 50-119 min.

There was evidence of hypothermia throughout the period of study (Table 3) but this fall in rectal temperature was statistically non significant. The heart rate and respiratory rate remained with in normal range following diazepam administration in neonatal calves (Table 3).

Table 3: Effect of diazepam on clinical and haematological parameters in neonatal calves (n=5, Mean±S.E)

Parameter	Base	Time interval after drug administration (min)					
	0 min	5	15	30	45	60	75
Rectal temp. (^oF)	101.0 ±0.35	100.5 ±0.55	99.4 ±0.85	95.8 ±3.55	96.4 ±2.8	95.8 ±3.56	95.6 ±3.52
Heart Rate Per min	94.4 ±5.38	100.0 ±7.87	102.4 ±6.93	88.8 ±3.65	92.0 ±3.75	86.4 ±4.32	87.2 ±3.27
Resp. Rate Per min	23.2 ±1.34	25.0 ±1.65	21.6 ±1.82	19.2 ±0.71	20.0 ±0.0	20.8 ±0.71	20.0 ±0.0
PCV (%)	29.85 ±3.52	----	33.2 ±1.76	30.46 ±2.01	32.36 ±2.77	31.28 ±2.96	30.96 ±3.75
Haemoglobin (g.%)	9.5 ±0.60	----	9.24 ±0.49	9.24 ±0.50	9.28 ±0.57	9.48 ±0.62	9.14 ±0.55
TEL Mlln/cmm	9.26 ±0.85	----	9.73 ±0.51	9.27 ±0.55	9.81 ±0.79	9.51 ±0.77	9.41 ±0.78
TLC 1000/cmm	38.72 ±4.96	----	40.5 ±10.8	32.16 ±7.46	31.32 ±9.74	19.88 ±4.5	32.02 ±9.7

b) Haematological Studies:

The effects of diazepam on various haematological parameters are shown in Table 3. No effect was observed in any of the haematological parameters studied in the present experimentation.

c) Biochemical Studies:

The effects of diazepam on different biochemical parameters are shown in Table 4. There was evidence of hyperglycaemia at 45 min interval but the rise in plasma glucose level was statistically non significant. The blood concentration of BUN, Creatinine, AST and ALT remained within normal range following diazepam administration ruling out any liver or kidney damage in the present study. Diazepam also failed to affect total protein and various electrolyte concentration of blood in neonatal calves.

Table 4: Effect of diazepam on biochemical parameters in neonatal calves (n=5, Mean±S.E)

Parameter	Base O min	Time interval after drug administration (min)				
		15	30	45	60	75
Glucose (mg/dl)	89.95 ±17.61	91.09 ±17.53	64.81 ±2.88	111.5 ±25.43	81.56 ±7.49	76.11 ±1.64
BUN (mg/dl)	14.52 ±2.25	11.45 ±2.48	8.33 ±0.81	14.02 ±3.58	11.96 ±3.10	13.9 ±2.23
Total proteins	4.96 ±0.61	4.76 ±0.29	4.45 ±0.32	4.64 ±0.39	5.54 ±0.54	4.7 ±0.27
Creatinine (mg/dl)	2.1 ±0.09	2.23 ±0.08	2.05 ±0.14	2.19 ±0.06	2.15 ±0.05	2.20 ±0.10
ALT (U/L)	9.6 ±0.96	10.4 ±1.15	11.0 ±0.63	14.0 ±2.17	11.4 ±1.76	9.8 ±0.91
AST (U/L)	33.0 ±2.28	35.00 ±5.84	24.25 ±4.36	32.4 ±4.98	32.2 ±4.29	34.2 ±4.59
Sodium (mEq/L)	132.6 ±3.63	133.4 ±3.08	135.8 ±2.03	134.8 ±2.32	132.0 ±3.08	132.8 ±1.07
Potassium (mEq/L)	6.92 ±0.81	7.32 ±0.84	7.3 ±0.81	7.0 ±0.94	7.22 ±0.88	7.24 ±0.95
Chloride (mEq/L)	112.54 ±15.7	94.8 ±3.76	100.9 ±2.26	123.0 ±12.94	116.7 ±18.76	112.77 ±118.71

D) EVALUATION OF TRIFLUPROMAZINE:

Trifluprомazine hydrochloride (Siquil) was evaluated in 8 male neonatal calves, 11-14 days old and weighing 16-24 kg. Three dose rates, 0.1 mg/kg and 0.5 mg/kg, I/V were used in three animals during pilot trials. On the subjective analysis, depending upon the sedation produced, a dose rate of 0.5 mg/kg, I/V, was standardized for evaluation in remaining five neonatal calves.

a) Sedative and Clinical Studies:

Following trifluprомazine administration, the onset and downtime (sternal) recorded were 3.50±0.75 min and 16.25±2.56 min, respectively. The recovery times recorded were 63.0±8.42 min (standing but ataxic) and 71.4±2.81 min (normal gait), respectively. In all the animals mild to moderate relaxation of neck and anal sphincter were observed. Relaxation of tail and jaws was not observed. There was mild to moderate depression of palpebral and corneal reflexes, observed only up

to 30 min interval. However reoccurrence of depression was noticed at 75 min interval. Mild depression of swallowing reflex, up to 30 min was seen only in two animals. Analgesia was absent following triflupromazine administration. Licking of muzzle and nearby objects, frequent urination and intermittent bellowing, ear shaking and sleepy look were common observations in all the neonatal calves during the study. Shivering was also noticed throughout the period of study. The peak effect remained for 46.75±11.5 min (14-67) whereas sedation was observed for 68.6±3.74 min (62-78) following triflupromazine administration in neonatal calves.

A significant (P<0.01) hypothermia was observed in all the animals (Table 5).

Table 5: Effect of triflupromazine on clinical and haematological parameters in neonatal calves (n=5, Mean±S.E)

Parameter	Base O min	Time interval after drug administration (min)				
		15	30	45	60	75
Rectal temp. (^{o}F)	101.5 ±0.19	100.3* ±0.34	99.1* ±0.57	98.7* ±0.55	98.6* ±0.62	98.6* ±0.53
Heart Rate Per min	88.4 ±2.56	116.0* ±9.80	100.0 ±5.37	98.8 ±4.96	100 ±5.66	97.6 ±7.86
Resp. Rate Per min	28.0 ±3.52	29.6 ±5.88	24.8 ±4.27	22.2 ±0.92	24.0 ±2.19	24.0 ±2.19
Haemoglobin (g.%)	9.4 ±0.64	9.68 ±0.83	9.48 ±0.77	9.44 ±0.76	9.52 ±0.75	9.26 ±0.77
PCV (%)	31.9 ±2.95	23.28 ±3.72	30.96 ±4.10	30.96 ±3.04	30.9 ±3.73	31.24 ±2.96
TEL Mlln/cmm	10.17 ±1.00	10.74 ±1.17	10.10 ±1.24	9.88 ±1.04	10.09 ±1.26	9.90 ±1.00
TLC 1000/cmm	16.06 ±3.66	26.92 ±6.97	16.46 ±4.46	25.0 ±6.19	17.32 ±3.54	20.62 ±5.41

*P<0.05

There was evidence of tachycardia (Table 5) up to 75 min interval but this increase in heart rate was significant only at 15 min interval. The respiration rate remained in their normal range (Table 5) following triflupromazine administration in neonatal calves.

b) Haematological Studies:

The effects of triflupromazine hydrochloride on different haematological parameters of neonatal calves are presented in Table 5. All the haematological parameters under study were not affected.

c) Biochemical Studies:

The effects of triflupromazine hydrochloride on different biochemical attributes of neonatal calves are presented in Table 6.

Table 6: Effect of triflupromazine on biochemical parameters in neonatal calves (n=5, Mean±S.E)

Parameter	Base O min	Time interval after drug administration (min)				
		15	30	45	60	75
Glucose (mg/dl)	64.6 ±7.20	83.1 ±12.04	81.5 ±6.51	69.15 ±13.01	78.56 ±11.56	80.3 ±9.70
Total proteins (g/dl)	5.58 ±0.20	5.72 ±0.32	4.48 ±0.54	6.26 ±0.97	5.52 ±0.48	5.50 ±0.52
BUN (mg/dl)	8.96 ±1.39	9.26 ±1.61	9.98 ±1.82	9.32 ±1.30	11.0 ±2.68	10.4 ±2.01
CRET (mg/dl)	1.33 ±0.23	1.59 ±0.22	1.45 ±0.26	1.34 ±0.24	1.19 ±0.30	1.18 ±0.33
ALT (U/L)	11.8 ±3.04	11.4 ±3.70	11.4 ±3.66	13.6 ±4.20	11.8 ±2.85	9.8 ±3.22
AST (U/L)	7.8 ±2.11	6.8 ±2.40	6.6 ±1.40	5.4 ±1.42	5.0 ±1.64	6.6 ±1.89
Sodium (mEq/L)	129.4 ±1.02	137.2 ±1.66	136.0 ±1.67	138.2 ±1.50	139.6 ±1.12	131.6 ±3.93
Potassium (mEq/L)	8.34 ±0.85	8.64 ±0.87	8.68 ±0.54	8.04 ±0.54	7.94 ±0.44	7.70 ±0.82
Chloride (mEq/L)	116.3 ±8.45	119.4 ±12.73	117.3 ±11.90	120.9 ±8.04	115.5 ±9.26	132.2 ±11.32

There was evidence of hyperglycaemia but statistically it was non significant (P>0.05). The BUN, Creatinine, AST and ALT concentrations remained within normal range following triflupromazine administration in neonatal calves ruling out the kidney or liver toxicity. No effect was observed on plasma total proteins and different time intervals were comparable to the base (hour) values.

E) EVALUATION OF ACEPROMAZINE MALEATE:

Acepromazine maleate was used in 9 male neonatal calves, 13-15 days old and weighing 22-26 kg. Four dose regimens, 0.1 mg/kg, 0.15 mg/kg, 0.5 mg/kg and 0.75 mg/kg, I/V or I/M, were used during the pilot trials. The sedative results were quite variable with all the dose rates and routes used during the study. The best sedation was achieved with @ 0.75 mg/kg when used intravenously. Since the sedation produced with acepromazine was quite variable, sometimes not seen even with higher dose rate, the detailed study of this tranquillizer was not done.

F) EVALUATION OF DETOMIDINE HYDROCHLORIDE

Effects of detomidine hydrochloride were evaluated in 8 male neonatal calves, 10 – 15 days old. The mean weight of calves of this group was 20.9 ± 1.37 kg. During pilot trials in three animals the dose rates of detomidine hydrochloride used were 0.015 mg/kg, 0.02 mg/kg and 0.03 mg/kg body weight, intramuscularly. At each dose rate two pilot trials were conducted. On subjective analysis, based on the extent of sedation, muscle relaxation and analgesia produced, the dose rates of detomidine standardized was 0.02 mg/kg, I/M and the same was used in remaining 5 neonatal calves to evaluate sedative, clinical, haematological and biochemical parameters.

Sedative and clinical studies:

The dose rate of detomidine hydrochloride standardized for neonatal calves was 0.02 mg/kg BW intramuscularly. The onset time and downtime recorded were 3.2 ± 0.39 min (Mean ± SE), 8.2 ± 0.08 min (sternal; Plate 2) and 26.5 ± 1.22 min (lateral), respectively. The recovery times recorded were 35-± 1.18 min (sternal), 85.2 ± 2.5 min (standing ataxia) and 95.2 ± 2.03 min (normal gait). The onset of effect was noticed within 2-4 min with peak effect remaining for 34.2 ± 7.99 min. In all the animals there was reoccurrence of deep sedation after first recovery, normally seen approximately after 35 min. Urination was a constant feature during recovery period. Licking of the muzzle, 1-2 min after detomidine administration, intermittent ear shaking and head resting on the ground during sedation were observed in all the animals.

In general there was moderate to complete suppression of ocular reflexes 30 min onwards till 75 min following detomidine administration. However, in one animal ocular reflexes were not affected. Detomidine hydrochloride produced moderate to complete muscular relaxation in all the animals as evidenced by relaxation of anal sphincter, jaws, neck and tail. The relaxation of anal sphincter was first to be noticed and last to come to normal during recovery period. The swallowing reflex was mild to moderately depressed up to 30 min of study. Detomidine hydrochloride failed to produce analgesia in present study except in one animal where mild analgesia was recorded up to 30 min only. In two animals initial mild salivation was also noticed.

The effects of detomidine hydrochloride on rectal temperature, respiration rate and heart rate are shown in Table 7.

Table 7: Effect of detomidine hydrochloride on clinical and haematological parameters in neonatal calves (n=5) Mean ± SE

Parameters		Minutes after detomidine				
(unit)	Base	15	30	45	60	75
Rectal Temp. (°F)	102.56 ± 0.30	102.88 ± 0.41	102.48 ± 0.31	101.96 ± 0.49	102.36 ± 0.36	102.44 ± 0.44
Heart rate (per min)	93.60 ± 3.32	73.60* ± 6.94	71.20** ± 4.72	75.20* ± 4.44	72.00* ± 6.69	70.40** ± 4.32
Resp. rate (per min)	33.60 ± 4.60	21.20 ± 1.56	30.80 ± 9.40	25.60 ± 6.05	20.80 ± 1.34	20.80* ± 1.75
Haemoglobin (g%)	8.06 ± 0.74	8.06 ± 0.84	8.06 ± 0.81	8.14 ± 0.75	7.78 ± 0.84	8.02 ± 0.81
PCV (%)	23.40 ± 2.77	24.30 ± 3.22	23.16 ± 3.08	25.14 ± 2.64	22.84 ± 2.96	20.54 ± 2.60
TEC (million/mm^3)	7.36 ± 0.73	7.67 ± 0.95	7.32 ± 0.83	7.88 ± 0.70	7.16 ± 0.83	6.52 ± 0.63
TLC (thous./mm^3)	8.20 ± 1.83	6.22 ± 0.48	9.98 ± 2.68	7.94 ± 1.20	6.56 ± 1.40	13.80 ± 4.32

** $P < 0.01$; * $P < 0.05$

There was no effect on rectal temperature during the period of study whereas decrease in respiration rate was observed from 15 min onwards till 75 min. However, the decrease in respiration rate was significant ($P< 0.05$) only at 75 min

interval. Detomidine hydrochloride produced a significant (P< 0.05) to highly significant (P< 0.01) bradycardia in the present study.

Haematological studies

Detomidine hydrochloride failed to produce any significant change in various haematological parameters in neonatal calves during the period of study (Table 7).

Biochemical studies

Highly significant (P < 0.01) hyperglycaemia was observed throughout the period of study (Table 8).

Table 8: Effect of detomidine hydrochloride on biochemical parameters in neonatal calves (n=5) Mean ± SE

Parameters		Minutes after detomidine				
(unit)	Base	15	30	45	60	75
Glucose	3.1400	97.22**	124.47**	107.75**	101.26**	109.10**
(mg/dl)		± 6.38	± 25.10	± 7.16	± 7.22	± 17.93
Total Protein	9.06	18.25	12.92	11.07	8.69	9.36
(g/dl)	± 2.77	± 2.20	± 1.37	± 2.19	± 2.74	± 1.43
BUN	7.58	9.11	9.53	9.26	8.64	7.94
(mg/dl)	± 0.62	± 0.80	± 0.84	± 0.69	± 0.42	± 0.54
Creatinine	2.93	2.39	2.46	2.54	2.72	2.33
(mg/dl)	± 0.24	± 0.16	± 0.19	± 0.10	± 0.29	± 0.28
AST	45.50	47.00	43.40	56.80	57.20	50.20
(U/L)	± 4.87	± 3.85	± 3.10	± 7.55	± 9.36	± 9.00
ALT	11.00	9.40	10.80	17.20	18.40	13.80
(U/L)	± 2.10	± 1.91	± 1.25	± 4.07	± 4.97	± 2.99
Sodium	96.80	92.40	92.40	104.80*	97.40	99.60
(meq/l)	± 1.93	± 7.24	± 4.25	± 1.68	± 3.69	± 3.55
Potassium	5.34	4.92	4.74	5.60	5.00	5.38
(meq/l)	± 0.27	± 0.53	± 0.18	± 0.50	± 0.49	± 0.41
Chloride	95.57	111.93	103.28	104.9	96.81	107.42
(meq/l)	± 6.08	± 9.33	± 3.94	± 9.25	± 4.05	± 8.64

**P < 0.01; *P < 0.05

There was evidence of hypernatraemia in the later stages of experimentation and increase in plasma sodium level was significant (P<0.05) at 45 min interval (Table 8). An increase in plasma total protein concentration was observed at 15, 30 and 45 min intervals following detomidine administration but the changes were statistically non-significant (Table 8). The changes in BUN, creatinine,

AST, ALT, potassium and chloride were not consistent and any change observed, was statistically not significant (Table 8).

G) <u>EVALUATION OF MEDETOMIDINE HYDROCHLORIDE:</u>

Dose rate of medetomidine hydrochloride was standardized @ 0.01 mg/kg body weight, intramuscularly by conducting pilot trials on five calves. The different dose rates of drug administered intramuscularly were as follow:

Pilot trial No.	(Dose rate mg/kg body wt.)
I	0.015
II	0.012
III	0.010
IV	0.075
V	0.010

Thereafter medetomidine hydrochloride @ 0.01 mg/kg body weight was evaluated in 6 neonate male calve, intramuscularly, on the basis of sedative, clinical, haematological and biochemical parameters.

Sedative studies and clinical studies:

The onset time recorded was 4 ± 0.63 minutes (Mean ± SE). The down time recorded was 10.17 ± 1.25 min. (sternal) and 14.6 ± 2.90 min (lateral) respectively. The recovery time recorded was 44 ± 5.78 (sternal), 81.8 ± 12.38 min. (standing but ataxic) and 107 ± 11.59min (normal gait). The maximum sedative effect remained for 40 ± 5.80 minutes whereas the peak effect remained for 30.41 ± 2.02 minutes.

FIGURES SHOWING SEDATION FOLLOWING MEDETOMIDINE ADMINISTRATION IN A NEONATE CALF.

Intermittent ear shaking and head resting on the ground during the sedation were commonly observed in all the animals. Micturition during sedation and after the recovery period was a constant feature. Recurrence of moderate sedation was observed normally 30 minutes after first recovery in all the animals.

Medetomidine hydrochloride produced mild to moderate depression of corneal reflex between 15 to 45 min intervals. In one animal corneal reflex was not affected. The palpebral reflex was not affected following medetomidine administration in all the animals. There was complete depression of swallowing reflex in three animals between 5 to 30 minutes, whereas in one animal it remained mildly depressed upto 75 minutes interval. Mild to moderate salivation was observed only in two neonate calves. Medetomidine administration failed to produce lacrimation in any of the animals in the present study. Mild to complete muscle relaxation, upto 45 minutes interval, was observed in two animals in the present study as evidenced by relaxation of anal sphincter, tail, jaws and neck. There was complete relaxation of anal sphincter and jaws between 5 to 30 minutes. The relaxation of anal sphincter and jaws was first to be noticed. However in two animal mild relaxation of anal sphincter remained upto 75 minutes interval. In general mild to moderate analgesia was noticed upto 30 minutes except in one animal where moderate analgesia remained upto 60 minutes interval as evidenced by no/ depressed response to deep pin pricks in neck and trunk (scratching of rib) areas of the animal. Downward deviation of cornea was observed during the study period in all the animals.

The rectal temperature ranged from 102.1 ± 0.38^0 F to 102.9 ± 0.36^0 F throughout the period of study and did not vary significantly from the base value of 102.6 ± 0.16^0 F (Table 9). Heart rate was significantly decreased ($P < 0.01$) immediately after injecting medetomidine hydrochloride at 5 minutes interval as compared to the pre-injected base values which persisted up to 75 minutes (Table 9). However, the respiration rate was insignificantly increased ($P > 0.05$) up to 15 minutes interval after medetomidine hydrochloride injection (29.0 ± 3.11 per minute) as compared to the base values (23.33 ± 2.29 per minute). Thereafter, it started declining and approached to the near base values.

Table 9: Effect of medetomidine hydrochloride on clinical parameters in neonatal calves (N = 6) Mean ± S.E.

Parameters		Minutes after medetomidine					
(Unit)	**Base**	**5**	**15**	**30**	**45**	**60**	**75**
Rectal temp. (^{0}F)	102.6 ± 0.16	102.7 ± 0.38	102.9 ± 0.36	102.7 ± 0.51	102.1 ± 0.38	102.3 ± 0.47	102.2 ± 0.44
Heart rate (/min)	88.00 ± 4.87	65.00** ± 6.18	66.16** ± 3.46	67.83** ± 1.22	67.33** ± 1.83	68.33** ± 1.96	68.66** ± 1.90
Resp.rate (/min)	23.33 ± 2.29	25.33 ± 1.52	29.00 ± 3.11	24.33 ± 0.88	23.66 ± 2.20	21.50 ± 2.22	24.16 ± 2.37

** $P < 0.01$

Haematological studies:

The haemoglobin (Hb) did not alter significantly after administration of medetomidine hydrochloride as compared to the pre-injected base values i.e. 10.15 ± 0.77 g% (Table 10).

Table 10: Effect of medetomidine hydrochloride on haematological parameters in neonatal calves (n = 6) Mean ± S.E.

Parameters		Minutes after medetomidine					
(Unit)	**Base**	**5**	**15**	**30**	**45**	**60**	**75**
Hb (g%)	10.15 ± 0.77	10.33 ± 0.80	10.46 ± 0.80	10.20 ± 0.72	10.16 ± 0.76	10.38 ± 0.90	9.86 ± 0.79
PCV (%)	45.00 ± 3.43	44.16 ± 3.80	45.00 ± 4.20	44.33 ± 4.15	44.16 ± 4.03	45.00 ± 4.49	45.16 ± 4.49
TEC (million/mm$^{3)}$	6.29 ± 1.64	6.55 ± 1.59	8.07 ± 1.74	8.01 ± 1.92	7.03 ± 1.82	6.22 ± 1.88	7.46 ± 2.49
TLC (Thous/mm$^{3)}$	9.92± 1.48	11.6± 2.06	10.67± 1.67	13.28± 3.29	11.27± 2.23	10.9± 2.28	9.16± 1.83

In all neonate calves, the packed cell volume (PCV) ranged from 44.16 ± 3.80 % to 45.16 ± 4.49 % throughout the period of study and did not vary significantly from the base values. Total erythrocyte count (TEC) remained increased insignificantly ($P > 0.05$) between 5 to 45 minutes and at 75 minute interval after medetomidine hydrochloride injection as compared to the pre-injected base values i.e. 6.29 ± 1.64 million/mm^3 (Table 10). Total leukocyte count (TLC) also showed an increasing pattern though insignificantly till 60 minutes interval after injecting medetomidine hydrochloride as compared to the base values (9.92 ± 1.46 thousand/ mm^3). It subsequently declined to 9.16 ± 1.83 thousend/mm^3 at 75 minutes. Maximum increase in the TLC values (13.28 ± 3.29 thousand/mm^3) was recorded at 30 minutes interval (Table 10).

Biochemical studies:

The effect of intramuscular administration of medetomidine on different biochemical parameters in neonate cow calves are presented in Table 11. The plasma glucose concentration was increased constantly till 30 minutes interval and reached to a significant level ($P < 0.05$) of 111.7 ± 16.77 mg/dL as compared to the base values (51.0 ± 2.67 mg/dL). It remained significantly higher up to 60 minutes, thereafter it was decreased to 100.2 ± 9.92 mg/dl at 75 minutes. Following medetomidine hydrochloride administration, there was an insignificant increase in the total plasma proteins (TP) concentration throughout the period of study. The blood urea nitrogen (BUN) and creatinine concentrations were remained decreased insignificantly ($P > 0.05$) after administration of medetomidine hydrochloride till the end of the experiment. Whereas, alanine aminotransferase (ALT) concentration remained increased insignificantly following administration of medetomidine hydrochloride. A slight increase in aspartate aminotransferase (AST) values was recorded between 15 to 75 minute intervals. The plasma sodium and potassium concentrations remained within normal range throughout the period of study whereas chloride concentration remained decreased insignificantly following administration of medetomidine hydrochloride till 75 minutes.

Table 11: Effect of medetomidine hydrochloride on biochemical parameters in neonatal calves (n = 6) Mean ± S.E.

Parameters		Minutes after medetomidine					
(Unit)	**Base**	**5**	**15**	**30**	**45**	**60**	**75**
Glucose (mg/dl)	51.00 ± 2.67	89.3 ± 17.24	100.3 ±10.22	111.7* ± 16.77	109.7* ±13.34	105.0* ± 14.34	100.2 ± 9.92
Total Proteins (g/dl)	4.51 ± 0.34	4.58 ± 0.31	4.75 ± 0.32	5.38 ± 0.25	5.26 ± 0.22	5.55 ± 0.47	5.08 ± 0.47
BUN (mg/dl)	13.81 ±1.13	12.25 ± 0.84	11.53 ± 2.41	12.28 ± 1.12	12.16 ± 1.20	11.16 ± 1.84	12.81 ± 0.47
Creatinine (mg/dl)	1.69 ± 0.22	1.66 ± 0.21	1.49 ± 0.15	1.66 ± 0.17	1.67 ± 0.24	1.50 ± 0.21	1.52 ± 0.21
ALT (U/L)	15.00 ± 1.46	16.00 ± 1.71	15.33 ± 1.30	15.16 ± 1.07	17.00 ± 1.37	16.00 ± 1.69	17.00 ± 1.59
AST (U/L)	44.00 ± 5.69	43.00 ± 5.13	46.00 ± 5.58	48.50 ± 7.70	45.66 ± 6.45	48.33 ± 5.00	46.00 ± 6.63
Sodium (meq/l)	133.0 ± 3.21	132.33 ± 3.07	131.33 ± 3.04	133.33 ± 3.78	132.00 ± 3.54	130.66 ± 3.99	132.3 ± 3.91
Potassium (meq/l)	3.93 ± 0.15	3.81 ± 0.17	3.78 ± 0.14	4.01 ± 0.28	3.93 ± 0.19	3.86 ± 0.21	4.05 ± 0.22
Chloride (meq/l)	102.0 ± 6.15	99.23 ± 5.11	96.66 ± 4.08	98.28 ± 3.89	95.98 ± 3.84	98.43 ± 3.11	94.95 ± 2.61

*P < 0.05

Depending upon the results achieved, xylazine hydrochloride (@ 0.22 mg/kg, I/M), detomidine hydrochloride (@ 0.02 mg/kg, I/M) and medetomidine hydrochloride (@ 0.01 mg/kg, I/M) proved as best pre anaesthetics (sedatives) for the neonatal calves. These drugs were further evaluated to see their effects on cardiovascular and electroencephalographic (EEG) parameters of neonatal calves.

Plate A : Comprehensive experimentation unit, showing monitoring of ECG, EEG and blood pressure in neonate calf following detomidine/detomidine-ketamine administration

CARDIOVASCULAR EFFECTS OF XYLAZINE HYDROCHLORIDE:

The cardiovascular effects of xylazine hydrochloride (0.22 mg/kg, I/M) were evaluated in 5 male neonatal calves, 10-15 days old and weighing 17-28 kg.

The effects of xylazine on various ECG parameters are presented in Table 12. There was gradual non-significant increase in QT, QoT interval and ST segment. P interval, PR interval, QRS complex and T interval were not affected following xylazine administration in neonatal calves. There was evidence of downward PR segment in three animals and elevation of ST segment in two animals. P wave became bifid in four animals after xylazine injection. At 30, 45 and 60 minutes intervals, following xylazine administration, there was a non-significant increase in T wave amplitude. No significant changes were observed in P wave and QRS complex amplitudes.

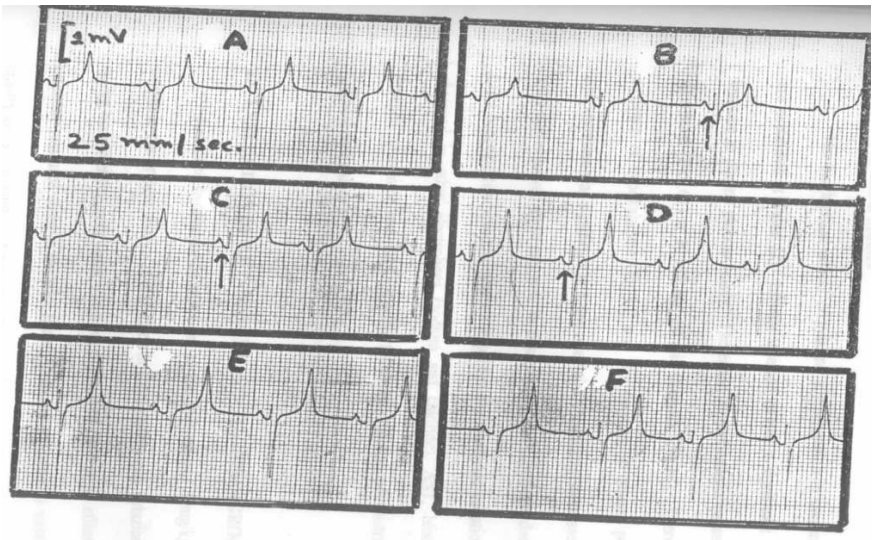

Fig. Electrocardiogram of a neonatal Cow calf following Xylazine administration showing downward PR segment (↑) and ST segment elevation.
A-Base; B, C, D, E, and F – 5, 15, 30, 45 and 60 min after Xylazine administration, respectively.

Table 12: Effect of xylazine anaesthesia on ECG parameters in neonatal cow calves (n=5, Mean±S.E).

Parameters	Base 0 min	Minutes after anaesthesia				
		5	15	30	45	60
P interval (seconds)	0.068 ±0.005	0.052 ±0.005	0.056 ±0.007	0.060 ±0.006	0.068 ±0.005	0.068 ±0.006
PR interval (seconds)	0.120 ±0.006	0.124 ±0.004	0.132 ±0.008	0.128 ±0.006	0.140 ±0.006	0.148 ±0.010
QRS complex (seconds)	0.076 ±0.004	0.072 ±0.008	0.068 ±0.008	0.080 ±0.000	0.076 ±0.004	0.068 ±0.005
QoT interval (seconds)	0.216 ±0.021	0.232 ±0.019	0.248 ±0.024	0.260 ±0.020	0.268 ±0.020	0.256 ±0.020
QT interval (seconds)	0.320 ±0.013	0.364 ±0.016	0.376 ±0.012	0.392 ±0.010	0.396 ±0.010	0.396 ±0.016
T interval (seconds)	0.104 ±0.015	0.132 ±0.023	0.132 ±0.015	0.132 ±0.015	0.128 ±0.021	0.124 ±0.010
ST segment (seconds)	0.140 ±0.025	0.160 ±0.020	0.180 ±0.021	0.184 ±0.019	0.192 ±0.021	0.188 ±0.021
P wave (mV)	0.090 ±0.029	0.110 ±0.019	0.110 ±0.019	0.110 ±0.019	0.120 ±0.020	0.110 ±0.019
QRS complex (mV)	-1.050 ±0.114	-1.170 ±0.195	-1.120 ±0.193	-1.020 ±0.183	-1.070 ±0.192	-1.070 ±0.252
T wave (mV)	0.630 ±0.068	0.600 ±0.055	0.670 ±0.097	0.730 ±0.151	0.760 ±0.144	0.700 ±0.214

Due to fault in the polyphyisiograph, the blood pressure and EEG could not be monitored in the neonate calves following xylazine administration.

CARDIOVASCULAR AND EEG EFFECTS OF DETOMIDINE HYDROCHLORIDE:

The cardiovascular and EEG effects of detomidine hydrochloride (0.02 mg/kg, I/M) were evaluated in 5 male neonatal calves, 10-15 days old and weighing 20.9 ± 1.37 kg.

Cardiovascular studies:

In the present study an initial rise in blood pressure, at 5 min interval, was recorded following detomidine administration in neonatal calves as evidenced by an increase in SP, DP and MAP values (Table 13). Thereafter hypotension was observed throughout the period of study. However, these changes in different parameters of BP were statistically non significant. PP was not affected (Table 13).

Table 13: Effect of detomidine hydrochloride on blood pressure in neonatal calves (n=5) Mean ± SE.

Parameter (unit)	Base	Minutes after detomidine					
		5	15	30	45	60	75
SP (mm Hg)	131.00 ± 7.17	133.00 ± 10.89	123.00 ± 10.08	119.00 ± 8.90	120.50 ± 8.08	126.00 ± 1.93	119.00 ± 5.39
DP (mm Hg)	119.00 ± 9.70	123.00 ± 10.84	110.50 ± 8.43	107.00 ± 10.64	109.00 ± 9.86	113.00 ± 3.05	104.50 ± 4.58
MAP (mm Hg)	123.00 ± 8.72	125.83 ± 10.35	114.89 ± 10.69	111.00 ± 9.69	112.89 ± 11.33	117.33 ± 1.84	106.67 ± 4.47
PP (mm Hg)	12.00 ± 4.13	10.00 ± 2.83	11.25 ± 3.70	12.00 ± 2.83	12.67 ± 2.25	13.00 ± 4.29	14.50 ± 4.10

SP = Systolic pressure; DP = Diastolic pressure; MAP = Mean arterial pressure
PP = Pulse pressure

The effect of detomidine hydrochloride on various ECG parameters in neonatal calves is presented in Table 14. In general an increase in different time interval parameters of ECG were recorded. However, these changes were statistically non significant. The P-wave and QRS-complex amplitudes were not affected. There was slight but statistically non- significant, increase in T-wave amplitude. In one animal a decrease in T-wave amplitude, throughout the period of study, and transient SA block were recorded at 60 min interval following detomidine administration (Fig.).

Table 14: Effect of detomidine hydrochloride on ECG parameters in neonatal calves (n=5) Mean ± SE.

Parameters (Unit)	Base	Minutes after detomidine					
		5	15	30	45	60	75
P-interval (sec)	0.056 ± 0.004	0.056 ± 0.012	0.068 ± 0.005	0.050 ± 0.008	0.055 ± 0.008	0.05 ± 0.007	0.055 ± 0.004
PR-interval (sec)	0.096 ± 0.007	0.100 ± 0.006	0.108 ± 0.008	0.112 ± 0.013	0.095 ± 0.008	0.100 ± 0.009	0.110 ± 0.011
QRS-interval (sec)	0.080 ± 0.009	0.088 ± 0.008	0.096 ± 0.013	0.108 ± 0.026	0.116 ± 0.026	0.104 ± 0.020	0.100 ± 0.017
QoT-interval (sec)	0.152 ± 0.016	0.160 ± 0.020	0.156 ± 0.016	0.180 ± 0.023	0.176 ± 0.025	0.118 ± 0.020	0.168 ± 0.021
T-interval (sec)	0.168 ± 0.015	0.176 ± 0.017	0.204 ± 0.016	0.192 ± 0.027	0.204 ± 0.019	0.200 ± 0.038	0.224 ± 0.031
QT-interval (sec)	0.320 ± 0.017	0.340 ± 0.014	0.344 ± 0.028	0.372 ± 0.015	0.364 ± 0.036	0.392 ± 0.035	0.392 ± 0.035
ST-segment (sec)	0.068 ± 0.008	0.076 ± 0.019	0.060 ± 0.015	0.080 ± 0.007	0.077 ± 0.014	0.105 ± 0.017	0.072 ± 0.016
P-wave (mv)	0.090 ± 0.010	0.080 ± 0.012	0.100 ± 0.039	0.087 ± 0.021	0.075 ± 0.013	0.080 ± 0.020	0.110 ± 0.056
QRS-complex (mv)	-0.850 ± 0.199	-0.870 ± 0.204	-0.740 ± 0.137	-0.710 ± 0.147	-0.810 ± 0.151	-0.860 ± 0.209	-0.740 ± 0.185
T-wave (mv)	0.580 ± 0.113	0.630 ± 0.185	0.710 ± 0.200	0.680 ± 0.211	0.714 ± 0.252	0.590 ± 0.146	0.600 ± 0.172

There was ST-segment depression in one neonate calf whereas ST-segment elevation in another.

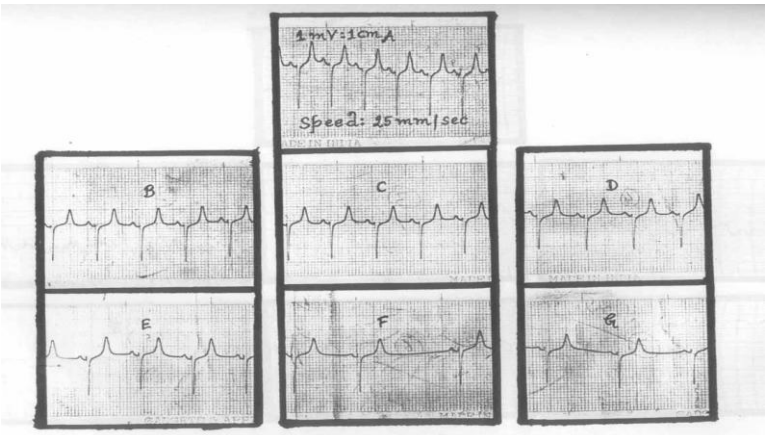

Fig. Electrocardiogram of a neonatal calf following detomidine administration showing decrease in T-wave amplitude throughout the period of study and SA-block at 60 min interval
A – Base; B, C, D, E, F and G – 5, 15, 30, 45, 60 and 75 min interval respectively

Electroencephalographic studies

Electroencephalographic studies revealed low voltage high frequency waves changing to low voltage low frequency waves (Fig.) following detomidine in neonatal calves and these changes were observed at 15 and 30 min interval only whereas in other two animals such changes were observed up to 75 min intervals. In one animal the normal low voltage high frequency waves changed to high voltage low frequency waves throughout the period of study.

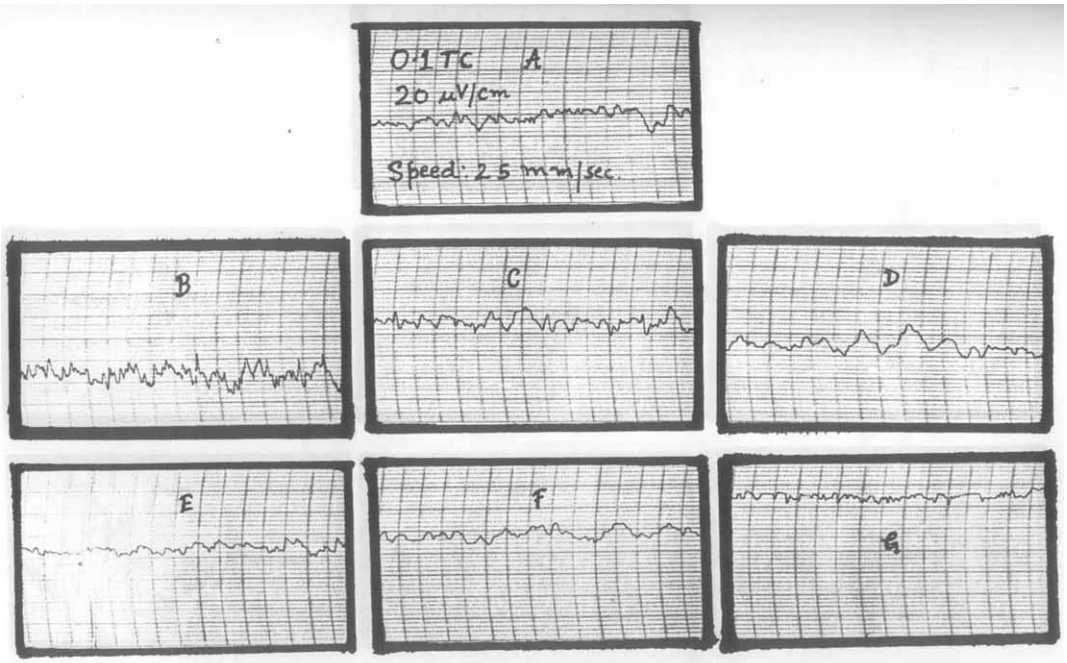

Fig. Electroencephalogram of a neonatal calf following detomidine administration showing low voltage low frequency waves throughout the period of study
A – Base; B, C, D, E, F and G – 5, 15, 30, 45, 60 and 75 min interval respectively.

CARDIOVASCULAR AND EEG EFFECTS OF MEDETOMIDINE HYDROCHLORIDE:

The cardiovascular and EEG effects of medetomidine hydrochloride (0.01 mg/kg, I/M) were evaluated in 6 male neonatal calves, 10-15 days old and weighing 20.17 $\pm$ 0.65 kg.

Cardiovascular studies:

A non-significant increase in systolic pressure (S.P) was observed at 5 minutes interval after administration of medetomidine hydrochloride as compared to the base values (Table 15) thereafter, it was decreased throughout the period of

study. However, this decrease was significant (P < 0.01/P < 0.05) at 30, 45 and 60 minute intervals. The diastolic pressure (D.P) and mean arterial pressure (M.A.P) showed a declining pattern after medetomidine hydrochloride administration throughout the period of study as compared to their respective base values. These values were significantly lower at 30, 45, 60 and 75 minute intervals. The pulse pressure (PP) was not altered significantly following administration of medetomidine hydrochloride at any interval.

Table 15: Effect of medetomidine hydrochloride on blood pressure in calves (n = 6) neonatal Mean ± S.E.

Parameters		Minutes after medetomidine					
(Unit)	Base	5	15	30	45	60	75
SP (mmHg)	125 ± 5.62	130.83 ±9.78	106.16 ±7.30	85.16** ±5.00	91.66** ±5.94	92.33* ±6.21	99.00 ±7.94
DP (mmHg)	105.00 ±6.70	100.00 ±11.32	85.50 ±6.84	62.50** ±4.88	69.50* ±6.79	68.00** ±6.02	73.83* ±9.31
MAP (mmHg)	111.67 ±6.25	110.27 ±10.34	92.39 ±6.90	70.05** ±4.85	76.89** ±6.48	76.11** ±5.76	82.22* ±8.85
PP (mmHg)	20 ±2.58	30.83 ±6.88	20.66 ±2.47	22.66 ±1.76	21.66 ±1.05	23.50 ±4.03	25.16 ±1.51

* P < 0.05; ** P < 0.01; SP = Systolic pressure; DP = Diastolic pressure
MAP = Mean arterial pressure: PP = Pulse pressure

Changes in electrocardiographic (ECG) parameters observed in neonatal calves after administration of medetomidine hydrochloride are presented in the Table 16. Significant to highly significant increase in QT-interval was recorded throughout the period of study. An increase in other ECG time parameters, except P-interval was also noticed following medetomidine administration in neonate calves but the change was statistically non-significant. In general there was a non-significant decrease in P-wave and T-wave amplitude and increase in the QRS- amplitude

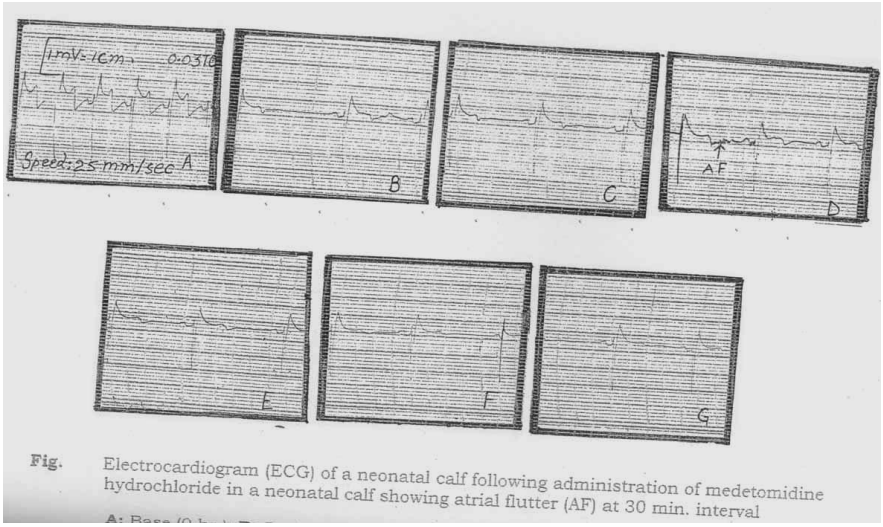

Fig. Electrocardiogram (ECG) of a neonatal calf following administration of medetomidine hydrochloride in a neonatal calf showing atrial flutter (AF) at 30 min. interval

Table 16: Effect of medetomidine hydrochloride on ECG parameters in neonatal (n = 6) calves Mean ± S.E.

Parameters		Minutes after medetomidine					
(Unit)	Base	5	15	30	45	60	75
P-interval (sec)	0.074 ±0.005	0.064 ±0.006	0.068 ±0.002	0.071 ±0.005	0.069 ±0.004	0.070 ±0.006	0.071 ±0.004
PR-interval (sec)	0.119 ±0.005	0.132 ±0.009	0.130 ±0.006	0.136 ±0.007	0.131 ±0.009	0.144 ±0.013	0.143 ±0.012
QRS- interval (sec)	0.103 ±0.010	0.137 ±0.017	0.148 ±0.020	0.138 ±0.015	0.147 ±0.020	0.143 ±0.019	0.143 ±0.016
Q_0T-interval (sec)	0.152 ±0.016	0.209 ±0.011	0.190 ±0.017	0.196 ±0.018	0.204 ±0.021	0.196 ±0.026	0.207 ±0.020
T-interval (sec)	0.156 ±0.022	0.161 ±0.018	0.187 ±0.018	0.209 ±0.011	0.195 ±0.013	0.207 ±0.028	0.183 ±0.023
QT-interval (sec)	0.302 ±0.008	0.371* ±0.015	0.374** ±0.012	0.406** ±0.016	0.396** ±0.014	0.416** ±0.024	0.390** ±0.007
ST-segment (sec)	0.045 ±0.007	0.066 ±0.019	0.045 ±0.007	0.056 ±0.004	0.051 ±0.004	0.058 ±0.004	0.061 ±0.011
P-wave (mv)	0.136 ±0.014	0.121 ±0.017	0.103 ±0.015	0.101 ±0.023	0.096 ±0.018	0.086 ±0.019	0.101 ±0.021
QRS-complex(mv)	-0.620 ±0.214	-0.563 ±0.167	-0.746 ±0.179	-0.771 ±0.179	-0.75 ±0.198	-0.761 ±0.210	-0.74 ±0.199
T-wave (mv)	0.405 ±0.060	0.220 ±0.084	0.253 ±0.092	0.263 ±0.151	0.268 ±0.129	0.225 ±0.135	0.236 ±0.126

*P < 0.05; **P < 0.01

throughout the period of study. ST-segment elevation and biphasic T-wave were recorded in all the animals. In one animal there was atrial flutter al 30 minutes interval following the administration of medetomidine hydrochloride (Fig.).

Electroencephalographic (EEG) studies:

Following medetomidine hydrochloride administration in neonatal calves, the EEG studies revealed low voltage high frequency waves changing to low voltage low frequencies waves at different time intervals (Fig.). Intermittent high voltage low frequency waves in the background of low voltage low frequency waves were also observed in three neonatal cow calves following medetomidine hydrochloride administration.

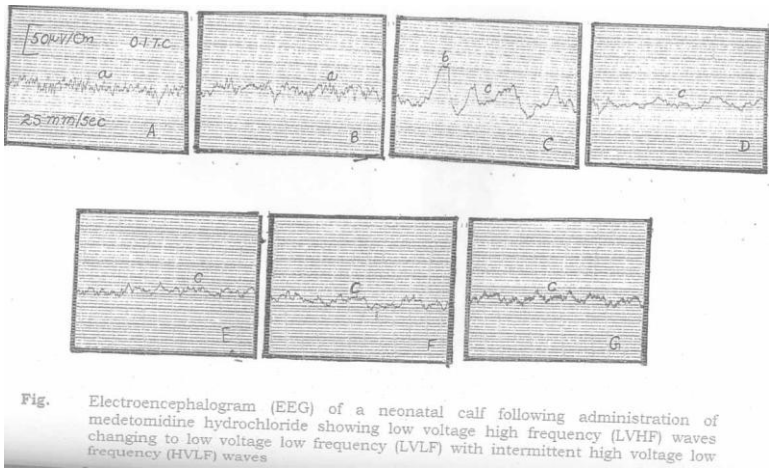

Fig. Electroencephalogram (EEG) of a neonatal calf following administration of medetomidine hydrochloride showing low voltage high frequency (LVHF) waves changing to low voltage low frequency (LVLF) with intermittent high voltage low frequency (HVLF) waves

H) EVALUATION OF CHLORAL HYDRATE:

Chloral hydrate was evaluated in 5 neonate male calves, 10-15 days old and weighing 23-27 kg. The dose rate computed for neonatal cow calves was 7.5 gm/100 kg bw, 4% solution, given by I/V route. The time of injection was 1.80 $\pm$ 0.27 minutes. Onset of effect was seen within 2-5 minutes with peak effect remaining for 17-25 minutes. There was recurrence of narcosis after 35 minutes in three animals and after 50 minutes in one animal. Normal gait was seen after 65-75 minutes in four animals and after 40 minutes in one animal.

Sedative and Clinical Studies:

There was mild to moderate suppression of palpebral and corneal reflexes. In one animal complete loss of palpebral and corneal reflexes was seen at 5

and 15 minute interval following chloral hydrate administration. Complete relaxation of neck, tail, anal sphincter and jaws was observed at 5 and 15 min intervals. However, relaxation was mild to moderate later on. In three animals, swallowing reflex was absent at 5 and 15 min intervals after chloral hydrate injection. There was mild to moderate analgesia of neck and trunk area, observed upto 30 minutes. Interdigital pinprick reflexes were not abolished in any of the animals following chloral hydrate administration. None of the animals revealed lacrimation or salivation after chloral hydrate.

There was gradual decrease in rectal temperature. The hypothermia was significant (P<0.05) at 15 min interval and highly significant (P<0.01) at 5, 30, 45 and 60 min intervals (Table 17).

Table 17: Effect of chloral hydrate anaesthesia on clinical and haematological parameters in neonatal cow calves (n = 5) Mean ± S.E.

Parameter (Unit)	Base	Minutes after anaesthesia				
		5	15	30	45	60
Temperature (^{o}C)	39.40 ±0.12	38.94** ±0.18	38.72* ±0.20	38.34** ±0.10	38.32** ±0.15	38.36** ±0.08
Heart rate (per min)	104.20 ±4.85	173.40 ±10.27	167.20 ±11.41	156.60 ±8.98	158.40 ±6.56	154.40 ±6.58
Resp. rate (per min)	16.40 ±1.40	24.60 ±1.49	21.40 ±0.78	18.80 ±0.72	19.00 ±0.80	18.60 ±1.49
Hb (g/dl)	11.72 ±0.60	ND	11.98 ±0.81	12.44 ±0.91	12.32 ±0.90	12.56 ±0.90
PCV (%)	37.60 ±2.22	ND	38.90 ±2.91	38.80 ±2.99	39.80 ±2.89	41.0 ±2.88

*P<0.05; **P<0.01; ND = Not done

Increase in heart rate was observed from 5 min interval till 60 minutes. These changes were highly significant (P<0.01) throughout the period of study (Table 17). Significant (P<0.05) increase in respiratory rate was seen at 5 min interval following chloral hydrate administration (Table 17). Thereafter the respiratory rate decreased gradually but the values remained above base (0 hour) values.

Haematological Studies:

A slight increase in haemoglobin and Haematocrit values was observed following chloral hydrate administration in neonatal cow calves, but the changes were non-significant (Table 17).

Cardiovascular Studies:

The effect of chloral hydrate on various ECG parameters is presented in Table 18.

Table 18: Effect of chloral hydrate anaesthesia on ECG parameters in neonatal cow calves (n = 5) Mean ± S.E.

Parameter (Unit)	Base	Minutes after anaesthesia				
		5	15	30	45	60
P interval (seconds)	0.068 ±0.004	0.060 ±0.008	0.065 ±0.005	0.060 ±0.006	0.060 ±0.006	0.056 ±0.009
PR interval (seconds)	0.116 ±0.004	0.100 ±0.008	0.115 ±0.005	0.116 ±0.004	0.116 ±0.004	0.132 ±0.007
QRScomplex (seconds)	0.080 ±0.006	0.076 ±0.011	0.080 ±0.009	0.080 ±0.006	0.072 ±0.005	0.084 ±0.007
QoT interval (seconds)	0.176 ±0.007	0.152 ±0.014	0.168 ±0.019	0.172 ±0.019	0.168 ±0.019	0.168 ±0.021
QT interval (seconds)	0.296 ±0.010	0.256 ±0.020	0.284 ±0.025	0.268 ±0.026	0.276 ±0.031	0.264 ±0.025
T interval (seconds)	0.120 ±0.006	0.104 ±0.010	0.116 ±0.010	0.096 ±0.007	0.108 ±0.013	0.096 ±0.010
ST segment (seconds)	0.096 ±0.011	0.076 ±0.019	0.088 ±0.023	0.092 ±0.019	0.096 ±0.021	0.084 ±0.022
P wave (mV)	0.120 ±0.012	0.150 ±0.035	0.138 ±0.024	0.110 ±0.019	0.100 ±0.016	0.080 ±0.012
QRScomplex (mV)	0.870 ±0.121	1.300 ±0.219	1.220 ±0.235	1.180 ±0.171	1.190 ±0.145	1.020 ±0.209
T wave (mV)	0.400 ±0.063	0.450 ±0.055	0.450 ±0.072	0.430 ±0.099	0.470 ±0.098	0.420 ±0.106

No significant changes were seen in different time interval and voltage parameters of electrocardiograms of different animals. ST segment elevation was a constant feature in all the animals following chloral hydrate administration (Fig.). There was initial increase in P wave amplitude (upto 15 minutes) but thereafter a decrease in T wave was seen. Chloral hydrate administration resulted in an increase in T wave amplitude and decrease in QRS complex amplitude. In one animal QRS

complex also increased. Transient SA block (5 & 15 minutes) was observed in one animal following chloral hydrate administration in neonatal cow calves.

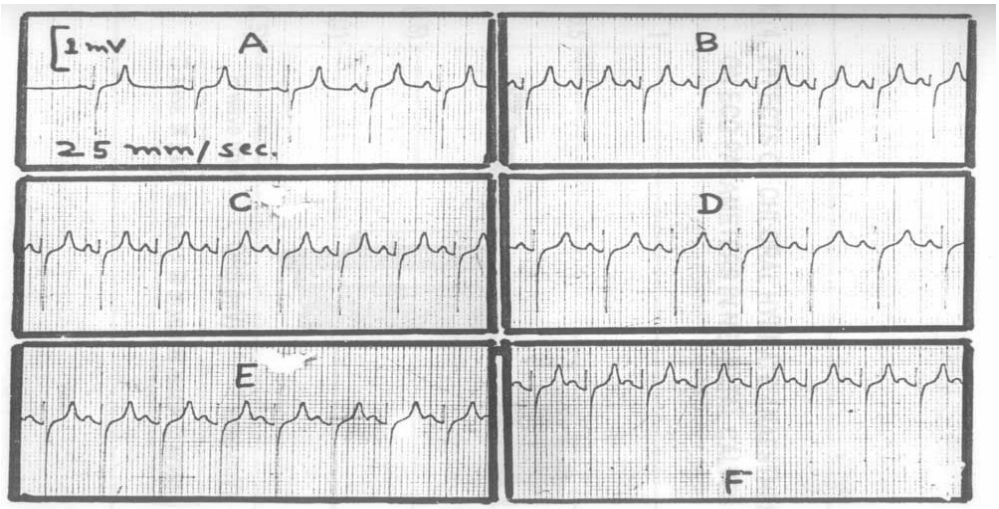

Fig. Electrocardiogram of a neonatal Cow calf following Chloral hydrate administration showing ST segment elevation throughout the period of study.
A-Base; B, C, D, E, and F – 5, 15, 30, 45 and 60 min after Chloral hydrate administration, respectively.

Biochemical Studies:

The effect of chloral hydrate on various biochemical parameters is presented in Table 19. None of the biochemical parameters except plasma glucose revealed significant changes in the present study following chloral hydrate administration. A significant ($P<0.05$) increase in plasma glucose levels with a non-significant increase in blood urea nitrogen levels was observed. A lot of variation was seen in LDH values in different animals and therefore a substantial increase in the concentration of the enzymes at 15 minute interval was also non-significant (Table 19). The rest of the blood biochemical parameters i.e. total proteins electrolytes (sodium, potassium and chloride), creatinine and liver function tests (AST and ALT), remained with normal range.

Table 19: Effect of chloral hydrate anaesthesia on plasma biochemical parameters in neonatal cow calves (n = 5) Mean ± S.E.

Parameter (Unit)	Base	Minutes after anaesthesia			
		15	30	45	60
Glucose (mg/dl)	79.00 ±4.26	89.00* ±5.39	86.20* ±4.37	85.80* ±3.53	89.80* ±4.03
Total Proteins (g/dl)	6.30 ±0.23	6.36 ±0.22	6.30 ±0.23	6.34 ±0.13	6.46 ±0.18
BUN (mg/dl)	8.40 ±0.92	9.20 ±0.66	9.70 ±0.77	10.88 ±0.37	10.00 ±1.02
Creatinine (mg/dl)	1.14 ±0.02	1.14 ±0.05	1.14 ±0.08	1.18 ±0.08	1.20 ±0.05
Sodium (mEq/L)	118.80 ±2.09	120.00 ±2.04	121.60 ±2.36	120.00 ±1.50	128.80 ±1.21
Potassium (mEq/L)	4.44 ±0.11	4.24 ±0.10	4.36 ±0.12	4.36 ±0.19	4.12 ±0.11
Chloride (mEq/L)	95.04 ±0.47	94.94 ±0.94	95.74 ±0.67	95.24 ±0.21	95.14 ±0.72
AST (U/L)	29.40 ±5.79	29.60 ±4.75	21.80 ±1.78	22.80 ±2.73	29.20 ±2.75
ALT (U/L)	9.80 ±1.04	10.20 ±1.11	10.00 ±0.85	8.40 ±0.73	9.60 ±1.51
LDH (U/L)	587.40 ±52.99	789.00 ±92.06	562.00 ±85.21	467.80 ±116.19	645.25 ±48.58

*P<0.05

I) <u>EVALUATION OF CHLORAL HYDRATE + MAGNESIUM SULFATE:</u>

Chloral hydrate + magnesium sulfate was evaluated in 5 neonate male calves, 10-15 days old and weighing 20-27 kg. The neonatal calves of this group received a combination of chloral hydrate and magnesium sulfate (Chloral-mag) in 1:1 ratio as 6% solution. The dose rate used was 10 gm/100 kg body weight by intravenous route. The time of injection was 30-80 seconds (Mean 49). The onset of effect was observed between 2-7 minutes with peak effect remaining for 8-39 minutes (Mean 25.4). However, the animals remained sedated for 45-60 minutes (Mean 54.0). This combination caused good muscle relaxation in neonatal calves but analgesia was not observed. Shivering was noticed in two animals at 45 and 55 minutes following chloral-mag administration. In one animal, initial laboured

respiration was observed after drug administration. All the neonatal calves were able to stand after experimentation but incoordination of gait was seen.

Sedative and Clinical Studies:

The chloral-mag combination resulted in a mild to moderate depression of palpebral and corneal reflexes with maximum depression seen at 15 minute interval. In one animal complete depression of corneal reflex was observed at 15 minute interval. Complete relaxation of neck and jaws was observed at 5 and 15 minute interval following infusion of chloral-mag combination whereas relaxation of tail and anal sphincter was moderate. The relaxation was mild at other intervals. There was mild to moderate depression of swallowing reflex. Analgesia was not observed in any of the animals receiving chloral-mag combination. Lacrimation and salivation were absent.

The combination resulted in progressive decrease in the rectal temperature of the neonatal cow calves. The decrease was significant ($P<0.05$) at 30 min and highly significant ($P<0.01$) at 45 and 60 minute intervals (Table 20).

Table 20: Effect of chloral-mag (1:1) anaesthesia on clinical and haematological parameters in neonatal cow calves (n = 5) Mean ± S.E.

Parameter (Unit)	Base	Minutes after anaesthesia				
		5	15	30	45	60
Temperature (^oC)	39.48 ±0.10	39.20 ±0.11	38.88 ±0.18	38.78* ±0.18	38.56** ±0.19	38.46* ±0.28
Heart rate (per min)	91.20 ±13.15	136.80* ±7.81	133.40 ±8.00	133.40 ±8.00	122.80 ±15.56	119.20 ±16.10
Resp. rate (per min)	20.00 ±1.67	24.60 ±4.74	22.40 ±2.48	22.40 ±2.48	16.00* ±1.05	15.40 ±1.44
Hb (g/dl)	7.88 ±0.17	ND	7.60 ±0.24	7.60 ±0.24	7.60 ±0.30	7.52 ±0.29
PCV (%)	39.60 ±3.12	ND	39.40 ±2.99	39.40 ±2.99	40.60 ±4.02	40.80 ±3.76

*P<0.05; **P<0.01; ND = Not done

The chloral-mag anaesthesia caused an increase in heart rate in calves. However, tachycardia observed in the present study, was significant only at 5 min interval (Table 20). Initially, there was non-significant increase in respiratory rate but later on oligopnea was noticed which was significant ($P<0.05$) at 45 min interval

(Table 20). However, respiratory rate remained within normal range throughout the period of experimentation.

Haematological Studies:

Chloral-mag combination didn't cause any specific change in haemoglobin and packed cell volume values in the neonatal cow calves (Table 20).

Cardiovascular Studies:

The effects of chloral-mag combination on various ECG parameters are presented in Table 21.

Table 21: Effect of chloral-mag (1:1) anaesthesia on ECG parameters in neonatal cow calves (n = 5) Mean ± S.E.

Parameter (Unit)	Base	Minutes after anaesthesia				
		5	15	30	45	60
P interval (seconds)	0.064 ±0.004	0.064 ±0.007	0.060 ±0.006	0.068 ±0.005	0.062 ±0.005	0.056 ±0.007
PR interval (seconds)	0.142 ±0.010	0.132 ±0.010	0.128 ±0.012	0.136 ±0.010	0.132 ±0.008	0.132 ±0.012
QRS complex (seconds)	0.048 ±0.005	0.056 ±0.004	0.052 ±0.005	0.048 ±0.005	0.056 ±0.004	0.054 ±0.004
QoT interval (seconds)	0.228 ±0.019	0.232 ±0.014	0.236 ±0.004	0.232 ±0.016	0.244 ±0.010	0.240 ±0.011
QT interval (seconds)	0.396 ±0.032	0.384 ±0.019	0.364 ±0.012	0.384 ±0.017	0.380 ±0.014	0.380 ±0.013
T interval (seconds)	0.168 ±0.015	0.152 ±0.015	0.128 ±0.010	0.152 ±0.005	0.136 ±0.007	0.140 ±0.009
ST segment (seconds)	0.180 ±0.015	0.176 ±0.015	0.184 ±0.004	0.184 ±0.012	0.188 ±0.010	0.182 ±0.007
P wave (mV)	0.080 ±0.012	0.120 ±0.025	0.110 ±0.019	0.100 ±0.016	0.080 ±0.012	0.100 ±0.016
QRS complex (mV)	0.980 ±0.178	1.010 ±0.203	0.980 ±0.213	0.930 ±0.191	0.940 ±0.178	0.900 ±0.204
T wave (mV)	0.190 ±0.043	0.230 ±0.037	0.200 ±0.032	0.240 ±0.024	0.200 ±0.065	0.210 ±0.037

ST segment elevation was a constant feature in all the animals in the present study. In one animal there was evidence of transient cardiac arrhythmia at 60 minute interval (Fig.). There was no variation in time and voltage parameters of ECG

following chloral-mag administration. However, in three animals, a non-significant increase in T wave amplitude was observed.

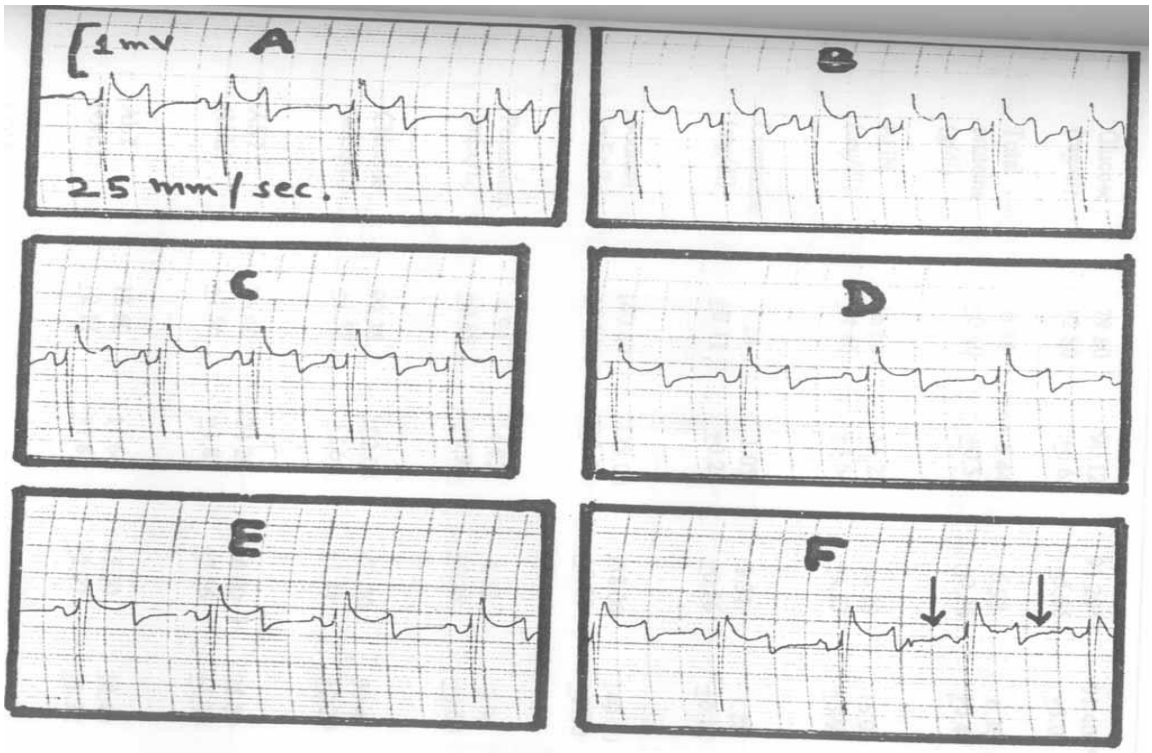

Fig. Electrocardiogram of a neonatal Cow calf following Chloral-mag (1:1) administration showing cardiac arrhythmia (F-waves) at 60 min interval (↓) and a constant ST segment elevation.
A-Base; B, C, D, E, and F – 5, 15, 30, 45 and 60 min after Chloral-mag administration, respectively.

Biochemical Studies:

The effects of chloral-mag anaesthesia on various biochemical constituents are presented in Table 22. There was a significant or a highly significant and gradual increase in the plasma glucose levels. Also an evidence of terminal hypokalaemia was observed in the present study, as there was a decrease in plasma potassium levels at 45 and 60 min interval. The concentrations of total proteins, BUN, creatinine, sodium, chloride, AST, ALT and LDH remained with normal range following chloral-mag administration in the neonatal cow calves.

Table 22: Effect of chloral-mag (1:1) anaesthesia on plasma biochemical parameters in neonatal cow calves (n = 5) Mean ± S.E.

Parameter (Unit)	Base	Minutes after anaesthesia			
		15	30	45	60
Glucose (mg/dl)	79.80 ±2.80	90.12* ±6.62	91.20** ±5.05	91.40** ±5.09	94.60* ±7.41
Total Proteins (g/dl)	6.48 ±0.40	6.44 ±0.51	6.92 ±0.36	6.36 ±0.49	6.68 ±0.49
BUN (mg/dl)	16.68 ±4.46	15.28 ±3.64	16.20 ±4.27	16.00 ±3.91	15.88 ±3.80
Creatinine (mg/dl)	1.28 ±0.11	1.05 ±0.25	1.31 ±0.16	1.28 ±0.12	1.22 ±0.15
Sodium (mEq/L)	140.80 ±0.80	138.00 ±3.03	138.00 ±0.89	140.00 ±3.10	144.00 ±1.67
Potassium (mEq/L)	4.94 ±0.89	4.82 ±0.92	4.52 ±0.88	3.96 ±0.60	4.16 ±0.60
Chloride (mEq/L)	99.38 ±1.58	102.04 ±2.61	101.30 ±1.11	99.42 ±2.29	102.60 ±3.30
AST (U/L)	26.40 ±1.96	24.20 ±1.83	26.60 ±2.56	25.00 ±1.14	24.80 ±2.58
ALT (U/L)	12.60 ±2.11	11.60 ±1.89	15.00 ±2.97	10.40 ±1.32	16.20 ±1.59
LDH (U/L)	767.20 ±119.50	822.40 ±84.90	896.60 ±42.80	723.40 ±89.50	794.60 ±115.20

*P<0.05; **P<0.01

J) EVALUATION OF CHLORAL HYDRATE-MAGNESIUM SULFATE-THIOPENTONE COMBINATION (CHLORAL-MAG-THIOPENTONE):

Chloral hydrate + magnesium sulfate and thiopentone sodium was evaluated in 5 neonate male calves, 10-15 days old and weighing 16-24 kg. Chloral-mag (1:1) was administered at the dose rate of 10 gm/100 kg body weight as 6% solution. Thiopental sodium (5%) was given 10 minutes later at a dose rate of 15 mg/kg body weight, 'to effect'. Both the anaesthetics were infused by intravenous route. In four animals, the anaesthesia was maintained with thiopental sodium (5%) at doses between 100-150 mg given at 15, 30, or 45 minutes after induction (Mean 131.25 mg, total) the said anaesthetic protocol was planned after pilot trials. The

chloral-mag-thiopental combination was not given as single solution for known reasons**.**

After thiopental injection onset of general anaesthesia was seen within 60 seconds with peak effect remaining 60 minutes or more (total period irrespective of maintenance). In one animal anaesthetic effect was seen for only 53 minutes, in which maintenance was not done. Breath holding was a common feature seen immediately after thiopental administration, which remained for 7-35 seconds (Mean 20.4). Initial effect (without maintenance) remained for 15-53 minutes (Mean 35.75). However, the neonatal cow calves remained under sedation or narcosis for more than 4 hours and complete relaxation was seen for more than 8 hours, even after 24 hours in two animals.

Sedative and Clinical Studies:

Chloral-mag-thiopental combination produced complete abolition of palpebral reflex between 5-60 minutes in all the neonatal calves. However, corneal reflex was mild to moderately suppressed except in one animal where it was completely abolished at 45 and 60 minute intervals. Relaxation of tail, neck, anal sphincter and jaws were complete throughout the period of study following chloral-mag-thiopental administration in cow calves. Similarly, complete abolition of swallowing reflex was noticed from 5-60 minutes in all the animals. There was complete analgesia of neck area. However, analgesia of trunk and interdigital space, though complete, remained from 5 to 45 minutes. At 60 minute interval analgesia of these areas was moderate. Mild lacrimation was observed at 15 minute interval in one animal following chloral-mag-thiopental anaesthesia. Salivation was scanty and was noticed throughout the period of study, but only in one neonatal cow calf.

The effects of chloral-mag-thiopental sodium anaesthesia on rectal temperature, heart rate and respiratory rate are presented in Table 23. A highly significant ($P<0.01$) hypothermia was observed. There was evidence of tachycardia, but the changes were non-significant. Respiratory rate remained within normal range when the values were compared to zero hour (base) values.

Table 23: Effect of chloral-mag-thiopentone anaesthesia on clinical and haematological parameters in neonatal cow calves (n = 5) Mean ± S.E.

Parameter (Unit)	Base	Minutes after anaesthesia				
		5	15	30	45	60
Temperature (^{o}C)	38.56 ±0.41	37.90** ±0.30	37.76** ±0.32	37.46** ±0.20	37.20** ±0.22	36.96** ±0.28
Heart rate (per min)	92.80 ±6.83	115.00 ±10.65	104.80 ±12.10	102.20 ±10.44	104.40 ±9.95	99.40 ±9.37
Resp. rate (per min)	24.00 ±4.06	28.40 ±5.16	25.00 ±2.49	24.40 ±2.84	25.60 ±3.19	26.20 ±2.84
Hb (g/dl)	8.86 ±0.90	ND	8.84 ±0.88	8.86 ±0.90	8.80 ±0.85	8.74 ±0.88
PCV (%)	34.40 ±5.01	ND	35.60 ±4.58	35.00 ±4.63	35.60 ±4.35	36.00 ±4.43

**P<0.01; ND = Not done

Haematological Studies:

No significant variations were noticed in haemoglobin and Haematocrit values of neonatal cow calves following chloral-mag-thiopental anaesthesia (Table 23).

Cardiovascular Studies:

The effects of chloral-mag-thiopental combination on various ECG parameters are presented in Table 24. There was slight, but non-significant, increase in QoT, QT and T wave intervals at 30, 45 and 60 minute intervals following drug administration in neonatal calves. A non-significant increase in ST segment interval was also noticed at 45 and 60 minute intervals. ST segment elevation was a constant feature in all the animals (Fig.). Biphasic T wave was noticed in all the animals. No significant changes were noticed in P, PR and QRS intervals and amplitudes of P wave, QRS intervals and amplitudes of P wave, QRS complex and T wave.

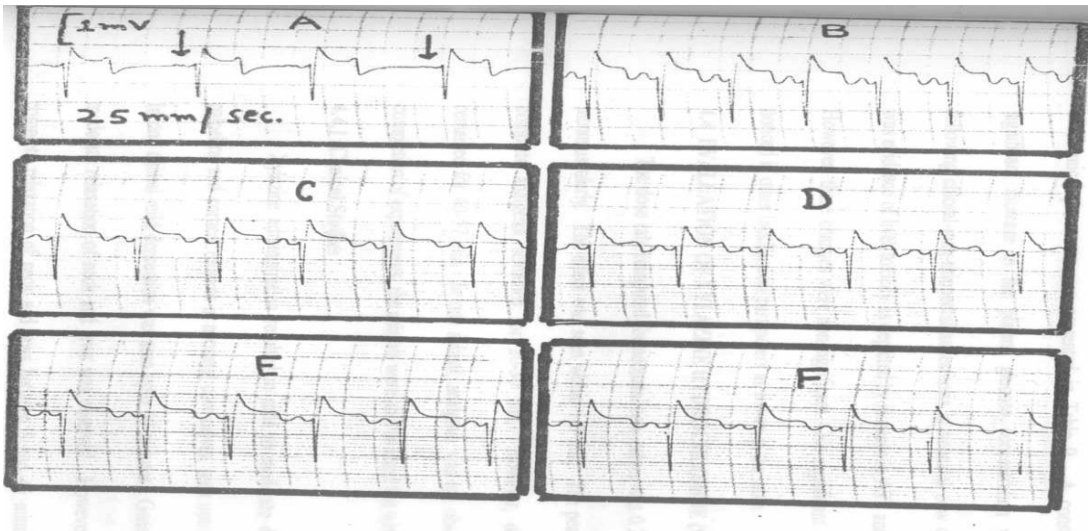

Fig. Electrocardiogram of a neonatal Cow calf following Chloral-mag-thiopentone anaesthesia showing bifid P wave (↓) before anaesthesia and ST segment elevation throughout the period of study.
A-Base; B, C, D, E, and F – 5, 15, 30, 45 and 60 min after Chloral-mag-thiopentone administration, respectively.

Table 24: Effect of chloral-mag-thiopentone anaesthesia on ECG parameters in neonatal cow calves (n = 5) Mean ± S.E.

Parameter (Unit)	Base	Minutes after anaesthesia				
		5	15	30	45	60
P interval (seconds)	0.064 ±0.004	0.072 ±0.005	0.068 ±0.005	0.064 ±0.004	0.060 ±0.000	0.064 ±0.000
PR interval (seconds)	0.128 ±0.008	0.128 ±0.005	0.120 ±0.013	0.124 ±0.012	0.120 ±0.009	0.124 ±0.007
QRS complex (seconds)	0.060 ±0.000	0.060 ±0.000	0.060 ±0.003	0.060 ±0.000	0.060 ±0.000	0.060 ±0.000
QoT interval (seconds)	0.268 ±0.005	0.272 ±0.027	0.264 ±0.025	0.268 ±0.025	0.280 ±0.024	0.292 ±0.027
QT interval (seconds)	0.416 ±0.012	0.424 ±0.041	0.416 ±0.029	0.444 ±0.047	0.456 ±0.051	0.464 ±0.053
T interval (seconds)	0.148 ±0.010	0.152 ±0.021	0.152 ±0.014	0.176 ±0.027	0.176 ±0.032	0.176 ±0.025
ST segment (seconds)	0.208 ±0.005	0.212 ±0.027	0.204 ±0.030	0.208 ±0.025	0.220 ±0.024	0.228 ±0.026
P wave (mV)	0.050 ±0.016	0.100 ±0.032	0.080 ±0.020	0.080 ±0.012	0.090 ±0.019	0.090 ±0.019
QRS complex (mV)	0.720 ±0.146	0.860 ±0.121	0.840 ±0.137	0.870 ±0.144	0.860 ±0.144	0.840 ±0.140
T wave (mV)	0.110 ±0.029	0.140 ±0.024	0.120 ±0.034	0.100 ±0.027	0.130 ±0.020	0.170 ±0.012

Biochemical Studies:

The effect of chloral-mag-thiopental anaesthesia on various biochemical parameters is presented in Table 25. A constant but non-significant increase in the plasma glucose concentration was observed following chloral-mag-thiopental anaesthesia in neonatal cow calves. There was evidence of liver toxicity as depicted by increase in AST and ALT values. However, these changes were non-significant. No significant changes were noticed in other biochemical parameters as shown in the table.

Table 25: Effect of chloral-mag-thiopentone anaesthesia on plasma biochemical parameters in neonatal cow calves (n = 5) Mean ± S.E.

Parameter (Unit)	Base	Minutes after anaesthesia			
		15	30	45	60
Glucose (mg/dl)	72.40 ±7.15	92.80 ±6.40	97.00 ±6.25	95.00 ±8.24	92.40 ±6.88
Total Proteins (g/dl)	4.56 ±0.57	4.76 ±0.46	4.94 ±0.61	4.64 ±0.58	4.88 ±0.67
BUN (mg/dl)	8.60 ±2.20	9.40 ±1.86	9.00 ±2.17	11.40 ±1.08	9.40 ±2.06
Creatinine (mg/dl)	1.20 ±0.13	1.04 ±0.07	1.16 ±0.22	1.06 ±0.09	1.10 ±0.16
Sodium (mEq/L)	138.80 ±6.71	141.20 ±2.87	140.80 ±4.32	135.60 ±3.12	137.20 ±0.80
Potassium (mEq/L)	4.70 ±0.29	4.84 ±0.45	4.54 ±0.29	4.22 ±0.21	4.38 ±0.17
Chloride (mEq/L)	88.68 ±2.51	91.10 ±1.69	88.68 ±2.60	89.92 ±1.20	90.36 ±1.50
AST (U/L)	36.80 ±3.84	40.00 ±3.74	38.60 ±4.82	47.80 ±8.56	37.20 ±7.14
ALT (U/L)	14.00 ±1.05	20.20 ±4.52	24.20 ±8.53	22.40 ±5.82	20.80 ±4.25
LDH (U/L)	484.40 ±61.86	442.00 ±53.09	623.40 ±124.37	544.40 ±51.31	438.0 ±65.66

K) <u>EVALUATION OF XYLAZINE-KETAMINE HYDROCHLORIDE:</u>

Xylazine + ketamine combination was evaluated in 5 neonate male calves, 10-15 days old and weighing 17-23 kg. Ketamine hydrochloride was used at the dose rate of 5 mg/kg body weight in the present study. It was given in combination with xylazine (0.22 mg/kg body weight) since there was a big problem of

cataleptic effect when ketamine was used alone in the pilot trials (4 animals). Both the anaesthetics were given simultaneously, in single syringe, by intramuscular route. The effect was seen within 1-5 minutes with peak effect remaining for 23-47 minutes. The animals remained under deep sedation for more than 60 minutes. Urination was seen at the end of the experiments in two animals. Transient cataleptic effect was also observed in two animals. There was grunting throughout the period of experiment in one animal. Respiration became very fast and shallow immediately after the administration of combination in all the calves. The animals were able to stand after 60 minutes but with ataxia.

Sedative and Clinical Studies:

In the present group receiving ketamine-xylazine combination, both, palpebral and corneal reflexes were depressed but the depression was mild to moderate seen between 5-45 minutes. In one animal corneal reflex was completely abolished at 15 min interval. Relaxation of neck and jaws was complete in all the animals, seen upto 45 minute interval. However, complete relaxation of tail and anal sphincter was seen only at 15 and 30 minute intervals. At 60 minute interval, there was mild relaxation of neck and jaws. In the present study the swallowing reflex was completely lost from 5-45 minutes following administration of the anaesthetics. There was complete analgesia of neck and trunk area between 15-45 minutes in all the neonatal interdigital space was only mild to moderate seen between 5 and 45 minute intervals. At 60 minute interval, analgesia was mild in all the animals. The combination of ketamine and xylazine didn’t cause lacrimation in any of the neonatal calves. However, there was mild to moderate salivation in all the animals at 5, 15, 30 and 45 minutes intervals.

Xylazine-ketamine combination caused a gradual decrease in rectal temperature in neonatal cow calves (Table 26). The decrease in rectal temperature was significant ($P<0.05$) at 30 and 60 min intervals and highly significant ($P<0.01$) at 45 minute interval (Table 10). In the present study, gradual decrease in heart rate

Table 26: Effect of xylazine - ketamine anaesthesia on clinical and haematological parameters in neonatal cow calves (n = 5) Mean ± S.E.

Parameter (Unit)	Base	Minutes after anaesthesia				
		5	15	30	45	60
Temperature (^{o}C)	39.50 ±0.10	39.23 ±0.09	39.15 ±0.09	38.98* ±0.05	38.70** ±0.07	38.65* ±0.12
Heart rate (per min)	100.83 ±7.15	85.33 ±4.76	82.33 ±2.38	75.33* ±2.74	65.50* ±1.47	66.17* ±1.82
Resp. rate (per min)	25.33 ±1.91	49.83* ±4.51	67.00* ±9.20	49.33* ±5.15	32.67 ±4.15	21.83 ±1.94
Hb (g/dl)	10.48 ±0.60	ND	10.24 ±0.58	10.00 ±0.45	10.04 ±0.56	10.00 ±0.56
PCV (%)	35.80 ±2.11	ND	34.40 ±2.38	33.20 ±2.69	33.20 ±2.69	33.80 ±2.42

*P<0.05; **P<0.01; ND = Not done

was observed from 5 min onwards till 60 minutes. Bradycardia was significant (P<0.05) at 45 and 60 minute intervals (Table 26). An abrupt and significant (P<0.05) increase in respiratory rate was observed following xylazine-ketamine administration at 5, 15 and 30 minute intervals. Thereafter, the respiratory rate was comparable to 0 hour (base) values (Table 26).

Haematological Studies:

There was a slight but non-significant decrease in haemoglobin and Haematocrit values following xylazine-ketamine administration in neonatal cow calves (Table 26).

Biochemical Studies:

The effects of xylazine-ketamine anaesthesia on various biochemical parameters in neonatal calves are given in Table 27. This combination resulted in a highly significant (P<0.01) increase in plasma glucose levels. A significant (P<0.05) decrease in ALT concentration was observed at 45 minute interval. The values of ALT were lowered further at 60 minute interval, but this decrease was non-significant. The xylazine-ketamine combination did not alter the plasma concentration of different electrolytes (sodium, potassium and chloride), total protein, AST, BUN and creatinine in neonatal calves, when the values were compared with zero hour (base) values.

Table 27: Effect of xylazine - ketamine anaesthesia on plasma biochemical parameters in neonatal cow calves (n = 5) Mean ± S.E.

Parameter (Unit)	Base	Minutes after anaesthesia			
		15	30	45	60
Glucose (mg/dl)	68.80 ±4.17	136.80** ±7.54	171.60** ±10.92	194.60** ±18.34	200.40** ±18.48
Total Proteins (g/dl)	6.34 ±0.24	5.96 ±0.25	6.08 ±0.21	6.06 ±0.23	6.34 ±0.35
BUN (mg/dl)	17.00 ±2.58	17.20 ±2.36	16.20 ±2.55	17.20 ±2.42	17.40 ±2.41
Creatinine (mg/dl)	1.40 ±0.13	1.36 ±0.15	1.32 ±0.15	1.32 ±0.14	1.28 ±0.13
Sodium (mEq/L)	133.20 ±3.72	131.00 ±5.74	133.00 ±5.61	133.60 ±3.81	133.40 ±5.20
Potassium (mEq/L)	4.84 ±0.43	4.34 ±0.43	4.48 ±0.42	4.52 ±0.33	4.64 ±0.36
Chloride (mEq/L)	98.32 ±1.07	97.10 ±1.50	98.32 ±1.31	99.02 ±1.40	98.20 ±0.89
AST (U/L)	47.60 ±3.75	43.40 ±2.92	43.40 ±2.41	42.20 ±2.20	40.40 ±3.18
ALT (U/L)	11.80 ±0.87	11.80 ±0.33	10.00 ±0.49	8.80* ±0.18	8.60 ±0.67
LDH (U/L)	678.20 ±56.96	590.60 ±61.94	648.20 ±72.85	648.20 ±109.10	593.80 ±89.52

*P<0.05; **P<0.01

Cardiovascular Studies:

The effect of xylazine-ketamine combination on various ECG parameters is presented in Table 28. There was significant (P<0.05) increase in PR, QoT and QT intervals at 30, 15 and 30 and 15 minutes, respectively. The increase in QoT and QT interval was noticed in ST segment interval. Similarly a significant or highly significant increase in P interval was also observed. However, QRS complex and T wave remained within normal range following xylazine-ketamine administration in calves when compared with base (0 hour) values. Slight ST segment elevation was observed in two animals (Fig.) whereas P wave became bifid in other two animals following anaesthetic administration.

Table 28: Effect of xylazine - ketamine anaesthesia on ECG parameters in neonatal cow calves (n = 5) Mean ± S.E.

Parameter (Unit)	Base	Minutes after anaesthesia				
		5	15	30	45	60
P interval (seconds)	0.052 ±0.005	0.064 ±0.004	0.064 ±0.006	0.060 ±0.006	0.052 ±0.005	0.060 ±0.006
PR interval (seconds)	0.112 ±0.005	0.128 ±0.005	0.124 ±0.004	0.132* ±0.008	0.120 ±0.000	0.128 ±0.005
QRS complex (seconds)	0.060 ±0.000	0.068 ±0.005	0.068 ±0.005	0.068 ±0.005	0.068 ±0.005	0.068 ±0.005
QoT interval (seconds)	0.208 ±0.014	0.228 ±0.005	0.248* ±0.005	0.260* ±0.006	0.284** ±0.012	0.288** ±0.005
QT interval (seconds)	0.308 ±0.014	0.328 ±0.005	0.340* ±0.006	0.364** ±0.013	0.392** ±0.010	0.388** ±0.015
T interval (seconds)	0.100 ±0.006	0.100 ±0.006	0.092 ±0.005	0.104 ±0.012	0.108 ±0.010	0.100 ±0.011
ST segment (seconds)	0.148 ±0.014	0.160 ±0.006	0.180* ±0.006	0.192* ±0.005	0.216** ±0.012	0.220** ±0.006
P wave (mV)	0.100 ±0.000	0.090 ±0.019	0.100 ±0.006	0.090 ±0.010	0.090 ±0.010	0.080 ±0.012
QRS complex (mV)	1.090 ±0.114	1.120 ±0.220	1.080 ±0.177	1.060 ±0.196	0.990 ±0.195	1.010 ±0.147
T wave (mV)	0.520 ±0.087	0.520 ±0.078	0.490 ±0.105	0.540 ±0.106	0.520 ±0.125	0.480 ±0.116

*P<0.05; **P<0.01

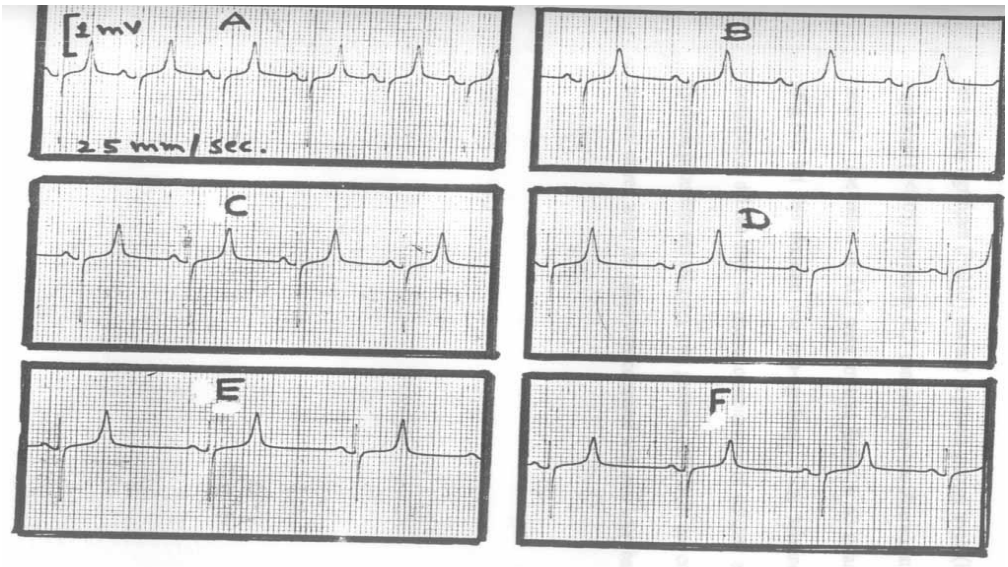

Fig. Electrocardiogram of a neonatal Cow calf following Xylazine-Ketamine anaesthesia showing slight ST segment elevation throughout the period of study.
A-Base; B, C, D, E, and F – 5, 15, 30, 45 and 60 min after Xylazine-Ketamine administration, respectively.

L) EVALUATION OF DETOMIDINE HYDROCHLORIDE AND KETAMINE HYDROCHLORIDE:

Effects of detomidine hydrochloride + ketamine hydrochloride, intramuscularly, were evaluated in 15 male neonatal calves, 10 – 15 days old. The mean weight of calves of this group was 20.2 ± 1.05 kg. During pilot trials the dose rates of ketamine used in combination with the computed dose of detomidine hydrochloride (0.02 mg/kg) were 5mg/kg, 7.5 mg/kg and 10 mg/kg. At each dose rate two pilot trials were conducted. On subjective analysis, based on the extent of sedation, muscle relaxation and analgesia produced, the dose rate of detomidine and ketamine standardized were 0.02 mg/kg and 7.5 mg/kg body weight, respectively.

Sedative and Clinical studies:

The animals of this group received a combination of detomidine hydrochloride and ketamine hydrochloride, simultaneously in a single syringe, by I/M route. The dose rates of these drugs standardized for surgical anaesthesia were 0.02 mg/kg and 7.5 mg/kg body weight, respectively. The onset and down time recorded were 1.6 ± 0.31 min and 2.0 ± 0.42 min (sternal) and 5.6 ± 0.80 min (lateral; Plate 3), respectively. Recovery time recorded was 48.6 ± 0.42 min (sternal), 88.2 ± 2.67 min (standing but ataxic) and 95.4 ± 2.63 min (normal gait). In all the animals the peak effect varied between 28 to 75 min. Licking of muzzle 1-2 min after detomidine-ketamine administration and during recovery period, intermittent twitching of eyelids, head shaking and twitching of muzzle were observed in all the animals. The relaxation of neck and anal sphincter were last to return to normal.

There was complete loss of ocular reflexes upto 45 min interval in three animals whereas in two animals mild to moderate depression was observed throughout the period of study. In four animals, complete relaxation of neck, tail, jaws and anal sphincter were observed upto 45 min interval following detomidine-ketamine administration in neonatal calves and thereafter the relaxation was mild to moderate. However, analgesia was complete only upto 30 min interval in these animals. In one animal there was complete relaxation and analgesia upto 75 min interval. There was moderate to complete depression of swallowing reflex upto 45 min interval in all the animals. Initial lacrimation (5 min interval) was observed in one animal.

Following detomidine-ketamine administration in neonatal calves there was significant ($P < 0.05$) to highly significant ($P < 0.01$) hypothermia at 45, 60 and 75 min interval (Table 29). A highly significant bradycardia was observed throughout the period of study whereas increase in respiratory rate was highly significant at 5, 15 and 30 min interval (Table 29). Thereafter there was an improvement in respiratory rate of the animals, which came to near normal at 60 and 75 min interval.

Table 29: Effect of detomidine hydrochloride and ketamine hydrochloride on clinical and haematological parameters (n=5) Mean ± SE

Parameters		Minutes after detomidine					
(unit)	Base	5	15	30	45	60	75
Temp. (°F)	102.60 ± 0.28	102.00 ± 0.26	102.10 ± 0.27	101.60 ± 0.46	101.20 * ± 0.38	100.90 ** ± 0.29	100.80 ** ± 0.31
Heart rate (per min)	97.60 ± 4.32	70.40** ± 3.85	76.00** ± 2.99	80.00** ± 1.13	81.60** ± 0.88	81.60** ± 1.83	81.60** ± 1.82
Resp. rate (per min)	31.20 ± 2.09	61.60** ± 2.68	72.80** ± 6.44	64.80** ± 8.19	45.60 ± 8.36	32.80 ± 3.65	29.60 ± 1.82
Haemoglobin (g%)	8.88 ± 0.97	ND	9.54 ± 0.85	9.40 ± 0.90	9.28 ± 1.04	9.38 ± 0.88	9.48 ± 0.88
PCV (%)	28.30 ± 3.06	ND	29.18 ± 3.13	29.54 ± 2.40	28.84 ± 3.86	28.62 ± 2.38	28.36 ± 3.27
TEC (million/mm^3)	7.61 ± 1.17	ND	9.21 ± 0.77	8.72 ± 0.66	10.29 ± 1.11	9.53 ± 0.92	8.91 ± 0.52
TLC (thous./mm^3)	14.07 ± 4.84	ND	13.44 ± 3.00	12.79 ± 1.90	13.08 ± 2.69	13.38 ± 2.33	15.66 ± 4.13

** $P < 0.01$; * $P < 0.05$; ND – Not Done

Haematological studies

All the haematological parameters like Hb, PCV, TLC and TEC remained within normal range following detomidine-ketamine administration in neonatal calves (Table 29).

Cardiovascular studies

In the present study, following detomidine-ketamine administration in neonatal calves, there was evidence of rising blood pressure upto 45 min interval only as depicted by an increase in SP, DP and MAP values (Table 30). However, increase in blood pressure was statistically non significant. The increase in pulse pressure was seen only at 5 min interval but it was not significant.

Table 30: Effect of detomidine hydrochloride and ketamine hydrochloride on blood pressure in neonatal cow calves (n=5) Mean ± SE

Parameters (unit)	Base	Minutes after detomidine					
		5	15	30	45	60	75
SP	110.00	136.00	116.40	115.60	113.60	110.40	109.20
(mm Hg)	± 3.29	± 4.60	± 6.05	± 4.53	± 6.14	± 10.46	± 3.01
DP	94.00	117.20	99.60	102.40	96.00	95.60	95.20
(mm Hg)	± 5.61	± 4.22	± 6.14	± 6.21	± 5.55	± 8.40	± 5.53
MAP	98.80	123.47	105.20	106.80	101.87	100.53	100.66
(mm Hg)	± 4.08	± 4.18	± 6.07	± 5.45	± 5.56	± 8.97	± 4.79
PP	16.80	20.50	16.80	13.20	17.60	14.80	14.00
(mm Hg)	± 3.72	± 2.24	± 1.50	± 3.61	± 3.19	± 3.72	± 5.02

SP = Systolic pressure; DP = Diastolic pressure; MAP = Mean arterial pressure
PP = Pulse pressure

The effects of detomidine-ketamine administration on various ECG parameters in neonatal calves are presented in Table 31. There was significant ($P < 0.05$) increase in PR interval at 15 and 75 min interval. The increase in PR interval was highly significant at 60 min interval. An increase in QoT interval, QT interval and ST segment was also observed but it was statistically not significant. The other time interval parameters of ECG were not affected. In the present study, there was an increase in QRS complex amplitude and a decrease in T-wave amplitude 5 min

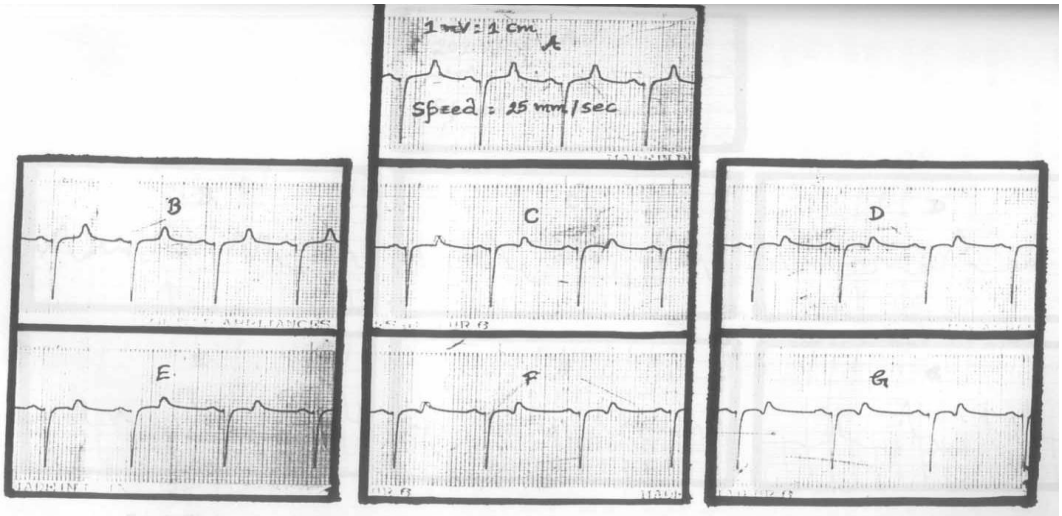

Fig . Electrocardiogram of a neonatal calf following detomidine-ketamine administration showing biphasic T-wave at 15, 30, 45, 60 and 75 min interval . A – Base; B, C, D, E, F and G – 15, 30, 45, 60 and 75 min interval respectively

Table 31: Effect of detomidine hydrochloride and ketamine hydrochloride on ECG parameters in neonatal calves (n=5) Mean ± SE

Parameters (unit)	Base	Minutes after detomidine + ketamine administration					
		5	15	30	45	60	75
P-interval (sec)	0.070 ± 0.005	0.080 ± 0.000	0.080 ± 0.000	0.080 ± 0.015	0.080 ± 0.001	0.080 ± 0.006	0.080 ± 0.004
PR-interval (sec)	0.120 ± 0.000	0.120 ± 0.004	0.130* ± 0.005	0.130 ± 0.009	0.130 ± 0.010	0.140** ± 0.004	0.130* ± 0.005
QRS-interval (sec)	0.090 ± 0.005	0.120 ± 0.013	0.120 ± 0.017	0.090 ± 0.008	0.090 ± 0.005	0.100 ± 0.007	0.090 ± 0.008
QoT-interval (sec)	0.150 ± 0.028	0.210 ± 0.015	0.180 ± 0.029	0.210 ± 0.015	0.200 ± 0.017	0.190 ± 0.026	0.180 ± 0.028
T-interval (sec)	0.250 ± 0.042	0.170 ± 0.019	0.280 ± 0.049	0.230 ± 0.034	0.220 ± 0.043	0.260 ± 0.060	0.260 ± 0.046
QT-interval (sec)	0.400 ± 0.016	0.380 ± 0.013	0.470 ± 0.020	0.440 ± 0.028	0.420 ± 0.032	0.440 ± 0.043	0.440 ± 0.028
ST-segment (sec)	0.060 ± 0.025	0.080 ± 0.023	0.100 ± 0.041	0.100 ± 0.027	0.100 ± 0.023	0.080 ± 0.025	0.080 ± 0.032
P-wave (mv)	0.100 ± 0.000	0.090 ± 0.011	0.100 ± 0.000	0.090 ± 0.011	0.090 ± 0.010	0.080 ± 0.012	0.090 ± 0.010
QRS-complex (mv)	-1.540 ± 0.143	-1.490* ± 0.186	-1.450 ± 0.199	-1.370 ± 0.188	-1.320 ± 0.630	-1.340 ± 0.132	-1.370 ± 0.145
T-wave (mv)	0.550 ± 0.066	0.410 ± 0.046	0.320 ± 0.087	0.350 ± 0.093	0.420 ± 0.108	0.450 ± 0.112	0.450 ± 0.105

** $P < 0.01$; * $P < 0.05$

onwards till 75 min. However, these changes were statistically not significant. The P-wave amplitude was not affected. In one animal, the T-wave became biphasic at 15, 30, 45, 60 and 75 min interval (Fig.).

Electroencephalographic studies

Following detomidine-ketamine administration in neonatal calves the electroencephalogram showed high voltage activity against the background of low voltage (Fig.) in comparison to low voltage high frequency activity seen before the

administration of drugs. These changes were consistent in almost all the animals and remained between 15 min onwards till 75 min.

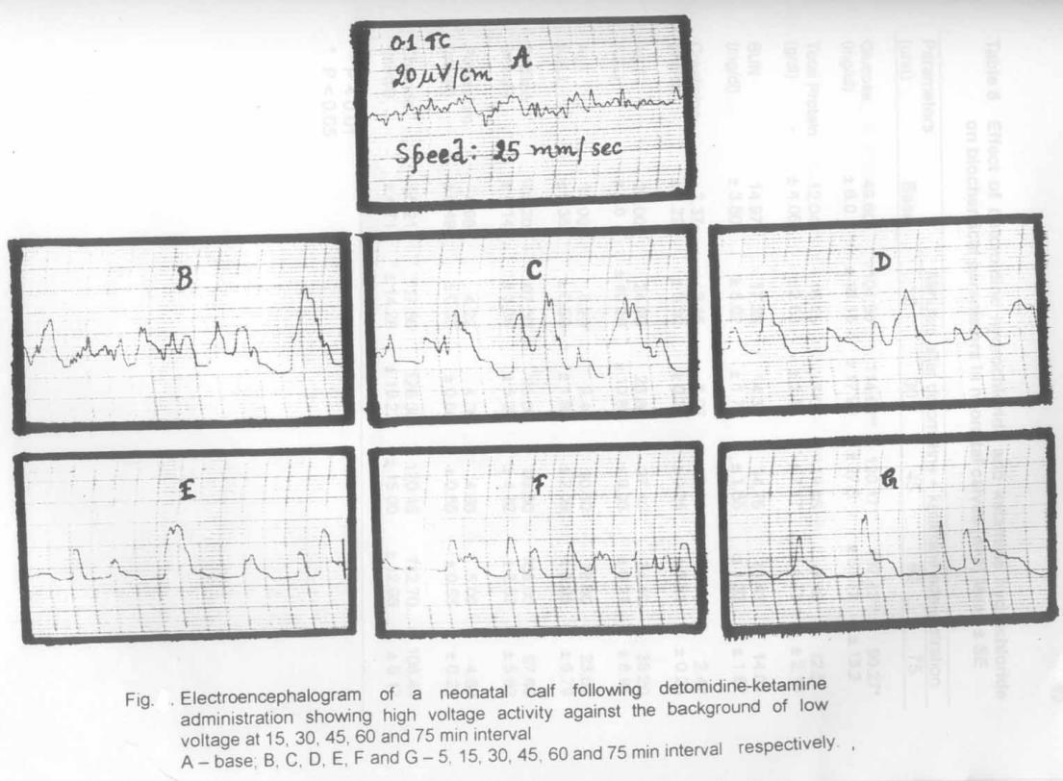

Fig. . Electroencephalogram of a neonatal calf following detomidine-ketamine administration showing high voltage activity against the background of low voltage at 15, 30, 45, 60 and 75 min interval
A – base; B, C, D, E, F and G – 5, 15, 30, 45, 60 and 75 min interval respectively.

Biochemical studies

The effects of detomidine-ketamine combination on different biochemical parameters in neonatal calves are shown in Table 32.

Significant ($P < 0.05$) to highly significant ($P < 0.01$) hyperglycaemia was observed throughout the period of study. A decrease in ALT was noticed up to 45 min interval, which was significant ($P < 0.05$) at 15 min interval. Thereafter the ALT values increased but these changes were statistically non-significant. A non-significant increase in AST concentration was also noticed at 45, 60 and 75 min interval. The changes in BUN, creatinine, sodium, potassium and chloride concentration were not consistent and were statistically non-significant.

Table 32: Effect of detomidine hydrochloride and ketamine hydrochloride on biochemical parameters in neonatal calves (n=5) Mean ± SE

Parameters		Minutes after detomidine + ketamine administration				
(unit)	Base	15	30	45	60	75
Glucose	49.60	104.50*	114.80**	120.17*	167.43**	90.27*
(mg/dl)	± 6.0	± 16.15	± 17.99	± 27.6	± 31.72	± 13.2
Total Proteins	12.04	16.15	7.06	19.46	9.46	12.57
(g/dl)	± 4.06	± 2.63	± 1.17	± 7.17	± 1.73	± 2.19
BUN	14.97	17.35	14.37	14.75	13.43	14.01
(mg/dl)	± 3.60	± 5.02	± 1.78	± 1.65	± 1.32	± 1.82
Creatinine	2.37	2.15	2.07	2.23	2.59	2.42
(mg/dl)	± 0.29	± 0.30	± 0.27	± 0.25	± 0.21	± 0.23
AST	23.00	24.00	23.80	27.40	34.40	35.20
(U/L)	± 7.6	± 10.28	± 10.88	± 9.03	± 6.21	± 8.81
ALT	13.00	8.20*	9.40	10.60	19.80	23.60
(U/L)	± 1.36	± 0.59	± 1.82	± 2.09	± 5.05	± 6.79
Sodium	102.20	97.00	95.00	99.60	105.00	97.80
(meq/l)	± 4.14	± 3.38	± 5.38	± 4.32	± 2.67	± 5.62
Potassium	4.98	4.22	4.36	4.66	5.00	4.60
(meq/l)	± 0.49	± 0.33	± 0.68	± 0.65	± 0.55	± 0.25
Chloride	95.21	117.86	128.30	120.15	112.70	106.44
(meq/l)	± 4.71	± 14.28	± 19.23	± 15.00	± 12.96	± 9.17

** P < 0.01; * P < 0.05

M) EVALUATION OF ATROPINE SULFATE + MEDETOMIDINE HYDROCHLORIDE AND KETAMINE HYDROCHLORIDE:

The present study was conducted on 19 apparently healthy neonatal male calves aged 10 to15 days and weighing 13 to 30 kg (20.47 ± 1.14) (Mean ± SE).

PILOT TRIALS:

Seven calves were used for pilot trials to standardize the dose of medetomidine hydrochloride in combination with ketamine hydrochloride. During pilot trials the dose rate of medetomidine hydrochloride used were 0.010 mg/kg and 0.015 mg/kg body weight. The dose rates of ketamine hydrochloride used in combination with computed dose of medetomidine were 5 mg/kg, 7.5 mg/kg and 10 mg/kg body weight. The different dose combination of the drugs medetomidine hydrochloride and ketamine hydrochloride in a single syringe were administered intramuscularly. The different dose combinations used during the pilot trials were as follows:

Pilot trial	Dose rate per kg body weight (I/M) Medetomidine hydrochloride	Ketamine hydrochloride
I	0.010 mg	5.0 mg
II	0.010 mg	7.5 mg
III	0.010 mg	7.5 mg
IV	0.010 mg	10.0 mg
V	0.010 mg	10.0 mg
VI	0.015 mg	10.0 mg
VII	0.015 mg	10.0 mg

Subjective analysis was adopted to standardize the dose of the drug combination. Based on the adequate extent of sedation, muscle relaxation and analgesia produced, the standardized dose rate of medetomidine hydrochloride and ketamine hydrochloride were 0.015 mg/kg body weight and 10.0 mg/kg body weight, respectively. There after the standardized combination was evaluated in two groups (Group 1 and 2), of six animals each.

Group 1: Evaluation of various sedative, analgo-clinical, haematological and biochemical parameters were carried out following intramuscular medetomidine + ketamine (single syringe) administration.

Group 2: Evaluation of various cardiovascular and electroencephalographic parameters was done following medetomidine + ketamine administration.

Sedative and clinical studies:

The onset time recorded was 1.16 ± 0.166 min (Mean ± SE) and down time recorded for sternal and lateral recumbency were 3 ± 0.73 min and 4.5 ± 0.50 min respectively following medetomidine + ketamine administration in neonate calves. Recovery time recorded were 79.33 ± 1.05 min (sternal), 108.16 ± 2.18 min (standing ataxia) and 128.5 ± 1.33 min (normal gait). Winking of eyes and flapping

of ears were observed 15-18 min after medetomidine + ketamine administration. Head shaking was noticed in all the animals. The relaxation of neck and anal sphincter were last to return to normal during recovery from anaesthesia. There was urination in three animals during recovery period. In four animals typical reoccurrence of deep sedation was observed, generally after 60 min of drug administration.

Following medetomidine + ketamine administration there was complete loss of corneal reflex at 5 , 15 and 30 min intervals in three animals, whereas in other three animals mild to moderate depression was observed upto 45 min intervals. In three animals, complete relaxation of neck, tail, jaws and anal sphincter was observed at 5, 15, 30 and 45 min intervals, following medetomidine + ketamine administration. The relaxation of anal sphincter was last to come to normal during recovery period. In five animals there was complete analgesia at 5 min interval, which persisted uptill 45 minutes, whereas in one animal moderate to complete analgesia remained uptill 60 min interval. There was complete depression of swallowing reflex upto 45 min through out the period of study following medetomidine + ketamine administration in four neonate calves. Lacrimation and salivation remained absent in all the animals.

There was indication of terminal hypothermia and bradycardia following medetomidine + ketamine administration in neonate calves but the changes were statistically nonsignificant (Table 33). However increase in respiratory rate was highly significant ($P < 0.01$) at 5, 15, and 30 min interval (Table33). Thereafter there was an increase in respiratory rate of the animals, which came to near normal at 60 and 75 min interval.

Haematological studies:

All the haematological parameters like Hb, PCV, TLC and TEC remained within normal range following medetomidine + ketamine administration in neonatal calves (Table 33).

Table 33: Effect of atropine - medetomidine + ketamine hydrochloride on clinical and haematological parameters in neonate calves (n=6) Mean ± SE

Parameters (unit)	Base	15 min aft.↓ atropine	Minutes after medetomidine + ketamine 5	15	30	45	60	75
Temp (^{0}F)	101.50 ± 0.39	101.80 ± 0.50	101.80 ± 0.62	101.40 ± 0.45	101.16 ± 0.51	100.70 ± 0.60	100.53 ± 0.53	100.83 ± 0.44
Heart rate (per min)	88.66 ± 4.52	93.00 ± 7.79	81.33 ± 7.01	85.33 ± 4.06	79.83 ± 5.71	76.00 ± 6.30	74.50 ± 6.38	78.50 ± 7.88
Resp.rate (per min)	25.50 ± 1.31	22.33 ± 2.17	59.83** ± 7.14	67.50** ± 10.80	76.83** ± 5.07	59.00** ± 4.50	43.00 ± 4.05	24.00 ± 2.45
Hb (g%)	09.00 ± 0.32	09.63 ± 0.33	10.23 ± 0.48	09.50 ± 0.35	09.36 ± 0.42	09.30 ± 0.58	09.43 ± 0.47	09.50 ± 0.56
PCV (%)	37.00 ± 2.11	38.33 ± 2.27	38.33 ± 2.09	37.33 ± 2.34	40.00 ± 2.12	39.00 ± 2.62	39.33 ± 2.10	39.66 ± 2.15
TEC (mill/mm^3)	8.48 ± 0.33	9.08 ± 0.23	9.14 ± 0.23	9.83 ± 0.36	10.05 ± 0.41	10.20 ± 0.34	9.14 ± 0.23	8.99 ± 0.24
TLC (thou./mm^3)	12.28 ± 1.01	13.30 ± 0.69	13.44 ± 1.10	12.32 ± 0.68	11.91 ± 0.95	12.49 ± 0.42	13.52 ± 0.62	12.93 ± 1.02

** $P < 0.01$; ↓ when medetomidine + ketamine administered intramuscularly.

Biochemical studies

The effect of medetomidine + ketamine combination on different biochemical parameters in neonate calves are shown in Table 34.

Highly significant ($P < 0.01$) hyperglycemia was observed almost through out the period of study. The plasma concentration of BUN increased following the administration of the drugs but the changes were statistically non significant (Table 34). The rest of the biochemical constituents viz. total proteins, creatinine, AST, ALT, sodium, potassium and chloride remained within normal range following medetomidine + ketamine administration in neonate calves.

Table 34: Effect of atropine - medetomidine + ketamine hydrochloride on biochemical parameters in neonate calves (n=6) Mean ± SE

			Minutes after - medetomidine + Ketamine					
Parameters (unit)	Base	15 min af.↓ atropine	5	15	30	45	60	75
Glucose (mg/dl)	64.83 ± 5.12	81.33 ± 4.63	114.16 ± 10.14	140.66** ± 18.52	155.33** ± 20.11	141.83** ± 16.34	149.50** ± 8.01	151.83** ± 16.01
TP's (g/dl)	4.76 ± 0.43	4.81 ± 0.43	4.55 ± 0.54	5.21 ± 0.55	4.73 ± 0.37	4.43 ± 0.48	4.93 ± 0.36	4.50 ± 0.37
BUN (mg/dl)	12.91 ± 1.63	16.38 ± 1.12	16.30 ± 1.48	16.13 ± 0.92	16.88 ± 1.14	16.65 ± 0.92	16.50 ± 1.04	16.46 ± 1.02
Creatinine (mg/dl)	1.52 ± 0.13	1.77 ± 0.12	1.63 ± 0.20	1.58 ± 0.22	1.59 ± 0.19	1.62 ± 0.15	1.59 ± 0.16	1.49 ± 0.15
AST (U/L)	34.83 ± 3.32	44.16 ± 5.04	34.33 ± 1.76	36.00 ± 3.30	34.66 ± 1.68	36.83 ± 2.62	37.83 ± 0.70	36.50 ± 1.33
ALT (U/L)	13.00 ± 0.51	11.33 ± 0.20	11.83 ± 0.74	11.16 ± 0.30	10.50 ± 0.50	10.33 ± 0.49	10.83 ± 0.48	12.00 ± 1.63
Sodium (meq/l)	124.66 ± 3.33	122.66 ± 3.88	121.33 ± 2.45	115.66 ± 7.23	119.67 ± 7.57	118.50 ± 5.01	121.50 ± 4.51	122.50 ± 4.42
Potassium (meq/l)	3.53 ± 0.24	3.43 ± 0.23	2.33 ± 0.21	3.35 ± 0.18	3.45 ± 0.14	3.35 ± 0.14	3.48 ± 0.21	3.60 ± 0.15
Chloride (meq/l)	93.25 ± 5.82	97.88 ± 3.28	95.08 ± 2.85	96.71 ± 4.00	97.10 ± 3.70	97.55 ± 4.79	100.86 ± 4.05	99.55 ± 3.80

** $P < 0.01$; ↓ when medetomidine + ketamine administered intramuscularly.

Cardiovascular studies

There was hypotension after the administration of the anaesthetic combination of medetomidine and ketamine hydrochloride in neonate calves, as indicated by significant (P< 0.05) to highly significant (P< 0.01) decrease in SP, DP

Table 35: Effect of atropine - medetomidine + ketamine on blood pressure in neonate calves (n=6) Mean ± SE

Parameters (unit)	Base	15 min af.↓ atropine	Minutes after medetomidine + ketamine 5	15	30	45	60	75
SP (mm Hg)	116.25 ± 5.54	123.75 ± 4.73	98.75 ± 10.87	69.50** ± 3.68	70.75** ± 1.70	78.00** ± 8.20	81.75** ± 4.80	87.75 ± 7.53
DP (mm Hg)	101.25 ± 7.73	108.75 ± 5.15	81.25 ± 12.64	54.50** ± 4.94	51.25** ± 4.53	59.50** ± 7.32	62.00** ± 5.22	67.50** ± 6.61
MAP (mm Hg)	106.24 ± 6.95	113.74 ± 4.73	87.07 ± 12.02	61.58** ± 4.99	57.74** ± 3.56	65.66** ± 7.59	68.58** ± 5.01	74.24* ± 6.74
PP (mm Hg)	15.00 ± 2.88	15.00 ± 3.53	17.50 ± 2.50	15.00 ± 2.04	17.00 ± 4.74	18.50 ± 1.50	19.75 ± 1.84	20.25 ± 3.42

SP = Systolic pressure; DP = Diastolic pressure; MAP = Mean arterial pressure; PP = Pulse pressure; **P < 0.01; *P < 0.05; ↓ when medetomidine + ketamine administered intramuscularly.

and MAP values at 15, 30, 45 and 60 min intervals in comparison to the base (0hr) values (Table 35). The fall in blood pressure was also recorded at 75 min interval but it was statistically non-significant (Table 35). A slight but non-significant (P> 0.05) increase in pulse pressure was also recorded at 30, 45, 60 and 75 min intervals following medetomidine + ketamine administration in neonate calves (Table 35).

The effects of medetomidine + ketamine combination on various ECG parameters in neonatal calves are presented in Table 36. There was an overall increase in different time interval parameters of ECG. However these changes were statistically nonsignificant. The P - wave and QRS - complex remained almost constant through out the period of study. The T - wave showed a decrease in

amplitude from 5 min interval till 75 min interval following medetomidine + ketamine administration but it was statistically nonsignificant.

Table 36: Effect of atropine - medetomidine + ketamine on ECG parameters in neonate calves (n=6) Mean ± SE

Parameters (unit)	Base	15 min af.↓ atropine	Minutes after medetomidine + ketamine 5	15	30	45	60	75
P-interval (sec)	0.059 ± 0.009	0.058 ± 0.008	0.053 ± 0.008	0.041 ± 0.010	0.046 ± 0.008	0.047 ± 0.008	0.053 ± 0.005	0.051 ± 0.009
PR-interval (sec)	0.130 ± 0.012	0.117 ± 0.010	0.131 ± 0.024	0.128 ± 0.022	0.135 ± 0.024	0.122 ± 0.016	0.134 ± 0.015	0.123 ± 0.013
QRS int. (sec)	0.124 ± 0.006	0.108 ± 0.010	0.126 ± 0.011	0.120 ± 0.017	0.116 ± 0.020	0.126 ± 0.013	0.129 ± 0.026	0.126 ± 0.015
Q_0T-interval (sec)	0.236 ± 0.029	0.186 ± 0.029	0.238 ± 0.028	0.238 ± 0.028	0.260 ± 0.032	0.256 ± 0.033	0.243 ± 0.033	0.256 ± 0.035
T-interval (sec)	0.190 ± 0.020	0.172 ± 0.026	0.202 ± 0.012	0.216 ± 0.036	0.214 ± 0.036	0.166 ± 0.019	0.252 ± 0.047	0.220 ± 0.050
QT-interval (sec)	0.426 ± 0.047	0.353 ± 0.028	0.441 ± 0.034	0.455 ± 0.060	0.474 ± 0.067	0.422 ± 0.047	0.495 ± 0.072	0.476 ± 0.077
ST-segment (sec)	0.112 ± 0.023	0.089 ± 0.033	0.112 ± 0.019	0.118 ± 0.018	0.147 ± 0.026	0.129 ± 0.020	0.113 ± 0.016	0.130 ± 0.024
P-wave (mv)	0.190 ± 0.020	0.172 ± 0.026	0.202 ± 0.012	0.216 ± 0.036	0.214 ± 0.036	0.166 ± 0.019	0.252 ± 0.047	0.220 ± 0.050
QRS Comp.(mv)	-1.166 ± 0.084	-1.066 ± 0.066	-1.150 ± 0.102	-1.083 ± 0.087	-1.150 ± 0.099	-1.100 ± 0.100	-1.200 ± 0.089	-1.183 ± 0.087
T-wave (mv)	0.096 ± 0.052	0.816 ± 0.012	0.050 ± 0.012	0.075 ± 0.024	0.058 ± 0.036	0.090 ± 0.036	0.088 ± 0.008	0.071 ± 0.017

↓ when medetomidine + ketamine administered intramuscularly.

In all the animals there was ST-segment elevation and biphasic T-wave before and after the administration of drugs/anaesthetics (Fig). In one animal atrial flutter was recorded at 75 min interval (Fig).

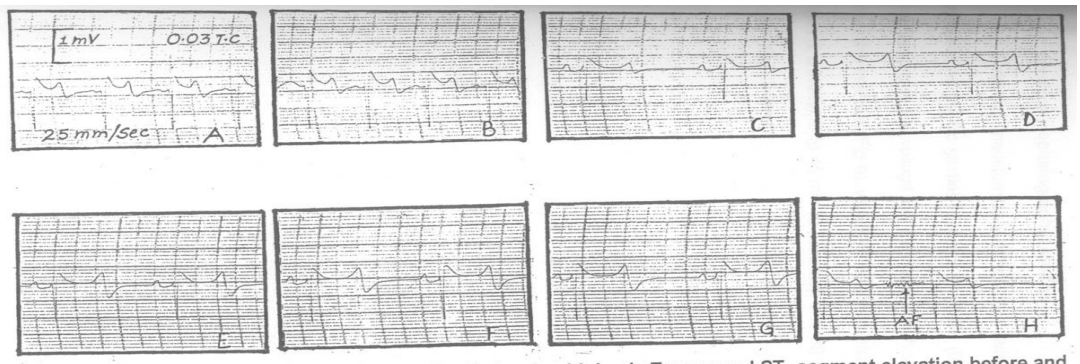

Fig 5: Electrocardiogram (ECG) of a neonatal calf showing biphasic T-wave and ST- segment elevation before and after the administration of atropine – medetomidine + ketamine anaesthesia.
A – Base (0hr); B – 15 min after atropinization; C, D, E, F, G, H – 5,15, 30, 45, 60 and 75 min interval respectively.
AF – Atrial flutter at 75 min interval.

Electroencephalographic studies

Following medetomidine + ketamine administration in neonate calves electroencephalographic studies revealed the base (0hr) low voltage high frequency waves changing to low voltage low frequency / high voltage low frequency waves at different time intervals (Fig), with burst suppressions recorded between 5 to 60 min intervals (2 animals), 5 to 45 min (2 animals), 5 to 30 min (1 animal) and at 5 and 15 min intervals (1 animal).

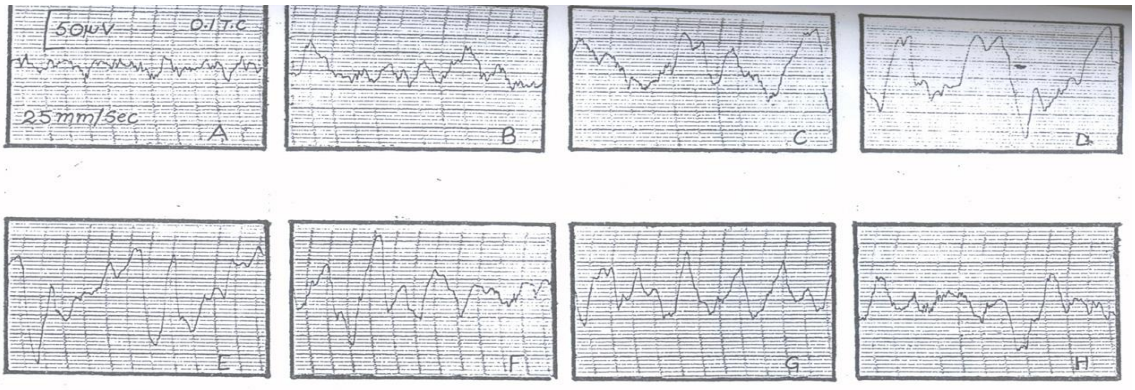

Fig 6: Electroencephalograph (EEG) of a neonatal calf following atropine – medetomidine + ketamine administration showing high voltage low frequency activity against the background of low voltage high frequency waves with intermittent burst suppression at 15 , 30 and 45 min interval.
A – Base (0hr); B – 15 min after atropinization; C, D, E, F, G, H – 5,15, 30, 45, 60 and 75 min interval respectively.

N) <u>EVALUATION OF DIAZEPAM PLUS THIOPENTONE ANAESTHESIA:</u>

The present study was conducted on 12 clinically healthy male neonatal cow calves aged 10-15 days and weighing 18 to 28 kg (22 ± 0.98) (Mean ± SE). These 12 calves were divided randomly into two groups (group I and group II) of six

animals each. The animals were comfortably secured in standing position and were administered atropine sulphate @ 0.04 mg/Kg subcutaneously, immediately followed by diazepam @ 0.3 mg/kg intravenously and followed 10 minutes later by thiopentone sodium (5%) intravenously “to effect”. The dose of thiopentone used “to effect” was found to be between 9.72 to 11.0 mg/Kg (10.2 ± 0.25 mg/Kg).

GROUP I: The six calves of this group were subjected for evaluation of sedative, clinical, haematological and biochemical studies following diazepam-thiopentone administration.

GROUP II: The six calves of this group were subjected for evaluation of cardiovascular and electroencephalographic studies.

Sedative and clinical studies:

All the animals were atropinized (atropine sulphate @ 0.04 mg/Kg, S/C) and immediately thereafter diazepam was given @ 0.3 mg/Kg by intravenous route in standing position. Thiopentone was given “to effect” 10 minutes after the administration of diazepam. After the injection of diazepam there was onset of ataxia followed by lowering of the head. The onset time recorded was 1.11 ± 0.26 minutes (Mean ± S.E). Thereafter the animals went into lateral recumbency. The down time recorded for lateral recumbency was 1.55 ± 0.33 minutes. After the administration of diazepam (3 ± 0.73 minutes) mild relaxation of anal sphincter and tail were observed in all the animals. The return to sternal recumbency was noticed 155.67 ± 4.61 minutes after administration of diazepam-thiopentone anaesthesia (Plate E). Animals made attempt to raise the head by 143.5 ± 2.37 minutes after administration of diazepam-thiopentone anaesthesia. Recovery times recorded were 354.83 ± 10.14 minutes (standing but ataxic) and 411.0 ± 15.96 minutes (normal gait). The duration of the effect of the combination (diazepam-thiopentone) remained for about 154.67 ± 4.59 minutes after the administration of anaesthetic agents. The complete abolition of corneal reflex was seen within 5 minutes after administration of thiopentone in all the animals. It remained absent between 5 to 45 minutes in two animals, 5 to 30 minutes in one animal, while in other three animals it remained absent between 5 to 15 minutes following administration of thiopentone.

There was complete abolition of palpebral reflex within 5 minutes after administration of thiopentone in all the animals. The palpebral reflex remains abolished upto 15 minutes post administration of thiopentone in all the animals except in one animal where it was observed up to 30 minutes. Photopupillary reflex was also abolished within 5 minutes after administration of thiopentone in all the animals. However in four animals the photopupillary reflex was abolished up to 30 minutes. Diazepam and thiopentone combination did not produce lacrimation, defecation or urination in any of the animals during whole period of study. Mild salivation was seen in only one animal, 2 minutes after the induction of anaesthesia with thiopentone. Mild cough reflex was noticed in two animals at 22.0 $\pm$ 6.9 minutes following administration of thiopentone. Intermittent twitching of ear was observed in two animals at 66.0 $\pm$ 6.0 minutes after the administration of thiopentone. The response to pin prick (rib scratching), used to determine the cutaneous analgesia, was diminished at 15.5 $\pm$ 0.76 minutes following administration of thiopentone (Plate D). Moderate to complete analgesia was observed for 5 to 15 minutes, after the administration of thiopentone in all the animals. Complete relaxation of neck, tail and jaws was noticed at 5 minute, which abolished at 75 minutes following administration of thiopentone. Mild to moderate relaxation of anal sphincter was observed 5 minutes after the diazepam administration but complete relaxation was noticed 5 minutes after the thiopentone administration, which continued upto 60 to 75 minutes in all the animals. Anal sphincter and neck were the last to return to the normal. Abolition of swallowing reflex was noticed immediately after induction of anaesthesia with thiopentone in all the animals, which remained so up to 30 minutes following administration of thiopentone in all the animals.

The effect of diazepam-thiopentone on rectal temperature, heart rate and respiratory rate in neonatal calves are shown in Table 37. There was no significant change in the rectal temperature after diazepam-thiopentone anaesthesia. However, a slight but non-significant hypothermia was noticed at 45, 60 and 75 minute intervals following thiopentone administration. A non-significant increase in the heart rate (tachycardia) was observed at 10 minutes after the diazepam administration and this increase remained up to 75 minutes following thiopentone

administration. Mild but non-significant rise in respiratory rate was noticed at 10 minutes after diazepam administration and subsequently the value gradually increased upto 75 minutes following administration of thiopentone.

Table 37: Effect of diazepam-thiopentone on clinical parameters in neonatal calves (n=6) Mean ± S.E.

Parameters (units)	Base Value	After diazepam (10 mins.)	Minutes after Thiopentone administration					
			5	15	30	45	60	75
Rectal Temp. (^{o}F)	102.8 ±0.31	102.7 ±0.36	101.7 ±0.69	101.1 ±0.66	101.1 ±0.55	100.9 ±0.64	100.7 ±0.63	100.7 ±0.63
Heart rate / minute	85.5 ±5.09	89.6 ±6.62	111.2 ±5.02	108.7 ±7.38	99.3 ±10.0	93.2 ±7.76	94.0 ±8.17	89.3 ±6.06
Respiration rate / minute	21.5 ±1.54	23.5 ±2.39	26.3 ±1.91	28.7 ±1.98	25.7 ±2.65	25.0 ±1.84	24.3 ±1.58	23.3 ±2.29

Haematological studies:

The effect of diazepam-thiopentone on various haematological parameters like haemoglobin (Hb), packed cell volume (PCV), total leukocyte count (TLC) and total erythrocyte count (TEC) in neonatal calves are shown in Table 38. There was no

Table 38: Effect of diazepam-thiopentone on haematological parameters in neonatal calves (n=6) Mean ± S.E.

Parameters (units)	Base Value	After diazepam (10 mins.)	Minutes after Thiopentone administration					
			5	**15**	**30**	**45**	**60**	**75**
Haemoglobin (gm %)	10.3 ±0.39	10.2 ±0.50	10.1 ±0.67	10.1 ±0.42	10.4 ±0.72	10.1 ±0.36	9.95 ±0.42	10.5 ±0.70
PCV (%)	43.2 ±2.63	42.3 ±2.79	44.5 ±3.01	45.2 ±3.18	43.8 ±3.42	47.7 ±3.73	45.2 ±4.51	46.7 ±4.89
TLC (thousands / mm^3)	9.02 ±0.71	7.92 ±0.59	8.45 ±0.65	7.74 ±0.86	8.54 ±0.81	7.92 ±0.4.0	7.94 ±0.62	8.59 ±0.81
TEC (million / mm^3)	5.43 ±1.93	5.78 ±2.00	6.28 ±1.96	5.68 ±2.05	6.09 ±1.86	5.56 ±2.09	5.79 ±2.30	5.27 ±1.81

significant change recorded in haemoglobin after diazepam-thiopentone anaesthesia during entire period of observations. A non-significant increase in PCV was noticed at 5, 15 and thereafter 45 to 75 minutes following thiopentone administration. A non-significant marginal decrease was observed in TLC at 10 minutes after diazepam and this decrease remained up to 75 minutes following thiopentone administration when compared to the base value. There was no significant alteration in the TEC throughout the period of study but slight increase was noticed at 5 and 30 minutes following thiopentone administration.

Biochemical studies:

The effect of diazepam-thiopentone on various biochemical parameters Table 39. The alteration in enzyme alanine aminotransferase (ALT) was not consistent i.e. at 10 minutes after diazepam an increase was observed whereas at 5 minutes following thiopentone administration it returned to near base value, thereafter increase was remained upto 75 minutes following thiopentone administration but was statistically non-significant. A non-significant decrease in aspartate aminotransferase (AST) enzyme level recorded at 10 minutes after diazepam administration and this decrease remained upto 75 minutes after administration of thiopentone. An increase in plasma sodium concentration was observed at 10 minutes after diazepam administration and it continued upto 75 minutes following thiopentone administration. A non-significant decrease in plasma potassium concentration was observed at 5 minutes after administration of thiopentone and which remained upto 75 minutes. A statistically non-significant decrease in plasma chloride concentration was noticed at 10 minutes after administration of diazepam which also remained upto 75 minutes after administration of thiopentone.

An increase in the blood glucose level (hyperglycaemia) was observed at 5 minutes after the administration of thiopentone. This statistically non-significant hyperglycaemia persisted up to 75 minutes following thiopentone administration. A marginal non-significant decrease in plasma total proteins at 60 minutes as compared to base value was recorded following thiopentone administration. The blood urea nitrogen (BUN) concentration decreased at terminal recordings when

compared to base value after diazepam-thiopentone administration. There was no significant change recorded in plasma creatinine during entire period of observations. The alteration in enzyme alanine aminotransferase (ALT) was not consistent i.e. at 10 minutes after diazepam an increase was observed whereas at 5 minutes following thiopentone administration it returned to near base value, thereafter increase was remained upto 75 minutes following thiopentone administration but was statistically non-significant. A non-significant decrease in aspartate aminotransferase (AST) enzyme level recorded at 10 minutes after diazepam administration and this decrease remained upto 75 minutes after administration of thiopentone. An increase in plasma sodium concentration was observed at 10 minutes after diazepam administration and it continued upto 75 minutes following thiopentone administration. A non-significant decrease in plasma potassium concentration was observed at 5 minutes after administration of thiopentone and which remained upto 75 minutes. A statistically non-significant decrease in plasma chloride concentration was noticed at 10 minutes after administration of diazepam which also remained upto 75 minutes after administration of thiopentone.

Cardiovascular Studies:

The effect of diazepam-thiopentone combination on blood pressure (systolic, diastolic and mean arterial) and electrocardiogram in neonatal calves are shown in Table 40 and Table 41, respectively. A statistically non-significant hypotension, as evidenced by decrease in systolic, diastolic and mean arterial pressures, was recorded at 10 minutes after administration of diazepam and remained upto 75 minutes following thiopentone administration. The change in pulse pressure was not consistent and was statistically non-significant. In one animal, immediately after administration of diazepam (0.3 mg/Kg, I/V) mean arterial pressure (MAP) dropped to 63.3 mmHg from the base value of 91.67 mmHg. However, after 10 minutes, the MAP recorded was 55 mmHg. Thiopentone administration sustained the decline in MAP upto 40 mmHg which resulted in sudden brain death of animal, however heart was working.

Table 39: Effect of diazepam-thiopentone on biochemical parameters in neonatal calves (n=6) Mean ± S.E.

Parameters (Units)	Base value	After Diazepam (10 min)	Minutes after Thiopentone administration					
			5	15	30	45	60	75
Glucose (mg/dl)	57.2 ±6.12	56.3 ±5.78	64.8 ±7.37	65.8 ±6.01	70.8 ±8.11	65.8 ±7.95	65.8 ±8.17	68.0 ±8.43
Total Protein (g/dl)	5.03 ±0.29	5.62 ±0.25	5.48 ±0.49	5.47 ±0.45	5.17 ±0.39	5.17 ±0.42	4.43 ±0.37	5.05 ±0.33
BUN (mg/dl)	23.5 ±9.63	23.2 ±9.85	22.8 ±10.1	22.4 ±9.33	22.7 ±9.64	23.2 ±10.1	21.8 ±9.35	21.3 ±8.69
Creatinine (mg/dl)	2.77 ±0.39	2.79 ±0.50	2.74 ±0.59	2.90 ±0.64	2.78 ±0.52	2.77 ±0.57	2.65 ±0.58	2.75 ±0.60
ALT (U/l)	14.8 ±1.6	17.0 ±2.1	14.8 ±1.3	16.0 ±2.5	15.1 ±2.0	15.5 ±2.0	16.5 ±3.9	15.5 ±2.2
AST (U/l)	48.3 ±4.43	45.7 ±3.01	47.3 ±4.49	43.3 ±2.98	42.5 ±3.35	44.0 ±3.31	44.0 ±4.12	41.5 ±3.75
Sodium (meq/l)	127 ±4.40	134 ±4.87	132 ±4.82	131.3 ±3.68	128.2 ±4.68	130.8 ±3.71	130.3 ±3.84	129.5 ±4.05
Potassium (meq/l)	4.08 ±0.34	4.1 ±0.35	3.85 ±0.34	3.78 ±0.28	3.71 ±0.25	3.87 ±0.36	3.72 ±0.21	3.72 ±0.28
Chloride (meq/l)	95.0 ±7.50	92.4 ±6.80	91.2 ±8.11	94.1 ±6.33	89.2 ±5.98	91.5 ±5.58	87.5 ±5.95	92.1 ±3.57

Table 40: Effect of diazepam-thiopentone on blood pressure in neonatal calves (n=6) Mean ± S.E.

Parameters (units)	Base Value	After diazepam (10 mins.)	Minutes after Thiopentone administration					
			5	**15**	**30**	**45**	**60**	**75**
SP (mmHg)	120 ±2.24	106.6 ±8.13	107.5 ±10.1	98.8 ±12.9	111.6 ±3.23	116.0 ±5.09	115.0 ±7.75	115.4 ±6.86
DP (mmHg)	102.5 ±4.79	91.7 ±7.81	95.8 ±10.9	81.5 ±13.9	95.0 ±3.53	101.6 ±5.7	101.0 ±7.81	100.0 ±5.47
MAP (mmHg)	108.3 ±3.64	96.6 ±7.87	99.7 ±10.6	89.4 ±11.6	100.5 ±3.33	106.3 ±5.40	105.6 ±7.77	105.1 ±5.90
PP (mmHg)	17.5 ±4.03	15.0 ±1.84	11.6 ±1.05	17.3 ±1.61	16.6 ±1.72	14.4 ±2.31	14.0 ±1.00	15.4 ±2.04

SP = Systolic Pressure; DP = Diastolic Pressure; MAP = Mean Arterial Pressure; PP = Pulse Pressure

There was no significant change in the ECG time and voltage component recorded after the administration of drugs during the entire period of observations, except for ST-segment elevation, some primary T-wave changes which include biphasic T-wave and inversion of T-wave (Fig.). These changes were recorded in all the animals. A non-significant decrease in PR-interval was noticed at 10 minutes after administration of diazepam and this decrease was seen from 30 to 75 minutes after the administration of thiopentone. Biphasic P-wave was also recorded in one animal. Slight but non-significant increase in P-wave amplitude was observed at 10 minutes following diazepam administration, which remained upto 75 minutes after the administration of thiopentone. In one animal inversion of T-wave was noticed at 5, 15 and 30 minutes following thiopentone administration (Fig.). A non-significant increase in T-wave amplitude was observed at 5 minutes after the administration of thiopentone, which remained upto 30 minutes. Thereafter it returned to near normal. This change was statistically non-significant. The changes in various other time and

voltage components (P-interval, QRS-interval, QT-interval, Q_oT-interval, T-interval and QRS-complex) were not consistent and statistically non-significant.

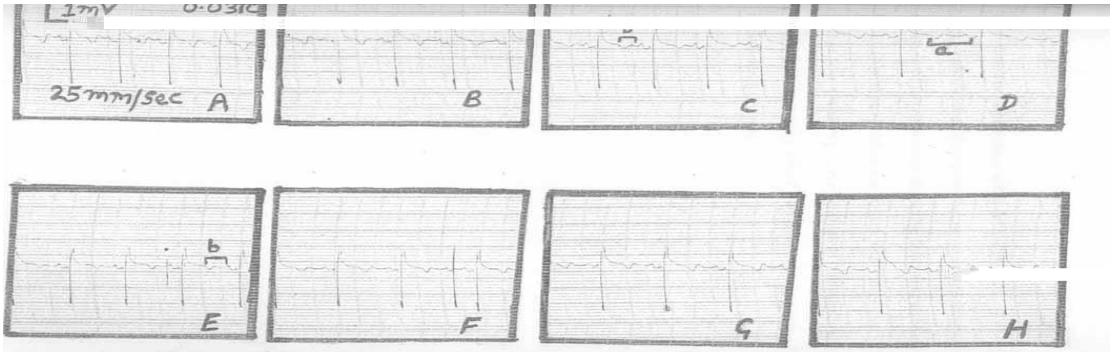

Fig. Electrocardiogram (ECG) of a neonatal calf following administration of diazepam-thiopentone anaesthesia in a neonatal calf showing biphasic T-wave and inversion of T-wave

A: Base (0 hr.); B: After diazepam (10 min.); C: 5 min; D: 15 min; E: 30 min; F: 45 min; G: 60 min; H: 75 min

a = Biphasic T-wave

b = Inversion of T-wave at 5, 15 and 30 min. following thiopentone administration

Electroencephalographic (EEG) studies:

The effect of diazepam-thiopentone anaesthesia in neonatal calves (n=6) are shown in Fig. Following diazepam-thiopentone administration in neonatal calves, the EEG studies revealed low voltage high frequency (LVHF) waves changing to low voltage low frequency (LVLF) waves at different time intervals. Intermittent high voltage low frequency (HVLF) waves in the background of LVLF waves were also recorded in 5 animals.

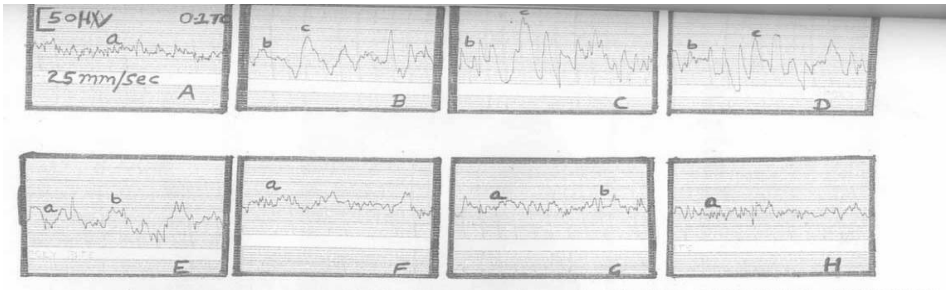

Fig. Electroencephalogram (EEG) of a neonatal calf following administration of diazepam-thiopentone anaesthesia showing low voltage high frequency (LVHF) waves changing to low voltage low frequency (LVLF) with intermittent high voltage low frequency (HVLF) waves

A: Base (0 hr.); B: After diazepam (10 min.); C: 5 min; D: 15 min; E: 30 min; F: 45 min; G: 60 min; H: 75 min

a = LVHF b = LVLF c = HVLF

Table 41: Effect of diazepam-thiopentone on ECG parameters in neonatal calves (n=6) Mean ± S.E.

Parameters (unit)	Base value	After diazepam (10 mins.)	Minutes after Thiopentone administration					
			5	15	30	45	60	75
P-interval (sec)	0.11 ±0.006	0.10 ±0.01	0.22 ±0.09	0.11 ±0.013	0.10 ±0.08	0.10 ±0.007	0.10 ±0.008	0.108 ±0.007
PR-interval (sec)	0.19 ±0.006	0.16 ±0.01	0.18 ±0.01	0.18 ±0.01	0.17 ±0.01	0.16 ±0.01	0.17 ±0.01	0.17 ±0.009
QRS-interval (sec)	0.08 ±0.01	0.08 ±0.01	0.08 ±0.007	0.08 ±0.01	0.09 ±0.01	0.09 ±0.01	0.08 ±0.01	0.09 ±0.02
QT-interval (sec)	0.35 ±0.02	0.34 ±0.01	0.34 ±0.01	0.35 ±0.03	0.35 ±0.02	0.36 ±0.02	0.35 ±0.02	0.36 ±0.02
Q_oT-interval (sec)	0.22 ±0.02	0.21 ±0.008	0.21 ±0.009	0.22 ±0.02	0.21 ±0.02	0.20 ±0.02	0.22 ±0.02	0.23 ±0.01
T-interval (sec)	0.15 ±0.02	0.17 ±0.01	0.16 ±0.01	0.16 ±0.03	0.16 ±0.02	0.17 ±0.01	0.17 ±0.02	0.16 ±0.03
ST-segment (sec)	0.05 ±0.01	0.04 ±0.006	0.04 ±0.01	0.03 ±0.01	0.05 ±0.01	0.04 ±0.01	0.05 ±0.01	0.02 ±0.006
QRS-complex (mv)	-0.63 ±0.10	-0.64 ±0.09	-0.65 ±0.09	-0.56 ±0.09	-0.68 ±0.06	-0.64 ±0.11	-0.64 ±0.08	-0.68 ±0.03
P-wave (mv)	0.10 ±0.01	0.14 ±0.04	0.14 ±0.03	0.11 ±0.03	0.12 ±0.03	0.11 ±0.03	0.14 ±0.03	0.12 ±0.04
T-wave (mv)	0.18 ±0.03	0.15 ±0.03	0.28 ±0.08	0.25 ±0.11	0.35 ±0.13	0.14 ±0.05	0.08 ±0.02	0.11 ±0.04

Summary:

Various sedatives/narcotics/anaesthetics were evaluated in 137 neonatal calves, 10-15 days old and weighing between 17-27 kg. All the animals were kept under same managemental conditions and were fed on milk. Water and milk were

withheld for 3 to 6 hrs prior to the experimentation work and each animal was weighed on the day of experiment.

Evaluation of atropine sulfate:

Atropine sulfate @ 0.04 mg/kg, used in 4 neonate calves did not produce any appreciable effect on heart rate. There was severe drying of muzzle and buccal cavity with polydypsia.

Evaluation of xylazine hydrochloride:

The evaluation of xylazine was carried out in 8 neonate calves. A dose of 0.22 mg/kg, IM was standardized for sedation. There was deep sedation for 40-57 min with peak effect and analgesia remaining for 20-30 min. The relaxation was mild to moderate with complete abolition of swallowing reflex. Salivation, tympani or regurgitation were not noticed. There was highly significant hypothermia and bradycardia with non-significant hyperpnea. Haematological parameters remained within normal range. ECG studies revealed gradual but non-significant increase in the QT, QoT and ST segment intervals with downward PR segment in three animals and ST segment elevation in other two. In four neonate calves P wave became bifid following xylazine administration. A highly significant hyperglycaemia was observed. There was evidence of hypokalaemia with a decrease in LDH and ALT concentrations.

Evaluation of Diazepam:

Diazepam was used in 8 male neonatal calves. On subjective analysis, depending upon the sedation produced, the dose rate of 0.3 mg/kg I/V was standardized for neonatal calves. There was sedation for 50-119 min with peak effect remaining for 7-35 min. Mild to moderate muscle relaxation was observed throughout the period of study. Salivation or relaxation was not observed. There was no analgesia. All the animals made violent efforts to stand during the sedation. There was evidence of hypothermia but heart and respiratory rates remained within normal range. No effect was observed in any of the haematological parameters studied. There was evidence of hyperglycaemia whereas other biochemical attributes remained within normal range.

Evaluation of Diazepam:

Triflupromazine hydrochloride was evaluated in 8 male neonate calves. Depending upon the sedation produced, a dose rate of 0.5 mg/kg, IV was standardized. The sedation was observed for 68.6±3.74 min (62-78) with peak effect remaining for 46.75±11.5 min (14-67). There was mild to moderate muscle relaxation without any analgesia. Hypothermia was significant with an evidence of tachycardia. The respiratory rate remained wit in normal range. All the haematological parameters monitored following triflupromazine administration were not affected. There was evidence of hyperglycaemia but statistically it was non significant. All other biochemical attributes remained with in normal range.

Evaluation of Acepromazine maleate:

Acepromazine maleate was tried for sedation in 9 neonate calves using different dose rates but the results obtained during these pilot trials were quite erratic. Therefore it is not recommended to be used for sedation in bovine neonate animals.

Evaluation of Detomidine hydrochloride:

The dose of detomidine hydrochloride (0.02 mg/kg, IM) was standardized and evaluated in two groups of 5 animals each. Detomidine hydrochloride induced sedation remained for 95.2 ± 2.03 min. However, peak effect was noticed for 34.2 ± 7.99 min. In all the animals there was reoccurrence of deep sedation after first recovery. Detomidine hydrochloride produced moderate to complete muscle relaxation in all the neonate calves. Ocular reflexes were moderate to completely depressed 30 min onwards till 75 min. There was mild to moderate depression of swallowing reflex upto 30 min. Detomidine hydrochloride failed to produce analgesia in the present study except in one animal in which mild analgesia was observed upto 30 min only. Initial mild salivation was observed in two animals only. Urination was a constant feature during recovery period. The rectal temperature remained within normal range. However, a decrease in respiration rate and bradycardia were noticed. Haematological parameters were not affected. Initial rise in blood pressure at 5 min. interval followed by a decrease in blood pressure were observed throughout the period of study. Detomidine hydrochloride resulted in non significant increase in different time interval parameters of ECG. P-wave and QRS

amplitude were not affected. There was slight but statistically non-significant increase in T-wave amplitude. Decrease in T-wave amplitude, transient SA-block at 60 min interval (one animal), ST-segment elevation (one animal), ST-segment depression (one animal) were the sporadic observations. EEG studies revealed low voltage high frequency waves changing to low voltage low frequency waves following detomidine administration in neonatal calves. Highly significant hyperglycaemia was noticed following detomidine. There was evidence of hypernatraemia in later stages of experimentation as a significant increase in plasma sodium was noticed at 45 min interval. Non-significant increase in plasma total protein was also observed at 15, 30 and 45 min intervals. The other biochemical attributes were not affected.

Evaluation of medetomidine hydrochloride:

Dose rate of medetomidine hydrochloride was standardized by conducting pilot trials on five healthy neonatal calves. Thereafter drug was administered @ 10μg/Kg body weight to conduct the study on 12 neonatal male cow calves. Study was divided into two groups and six animals were used in each group. In neonate calves, sedation was induced within 4.0 ± 0.63 minutes following intramuscular administration of medetomidine hydrochloride. The induced sedation remained for a period of 40 ± 8.50 minutes and the peak effect of sedation was 30 ± 1.25. However, relapse of moderate sedation was observed after first recovery. In general mild to moderate analgesia was noticed upto 30 minute intervals except in one animal where moderate analgesia remained upto 60 minutes interval as evidenced by no/depressed response to deep pin prick in neck and trunk (scratching of rib) area of the animal. Medetomidine hydrochloride produced mild to complete muscular relaxation up to 45 minutes interval. There was complete relaxation of anal sphincter and jaws between 5-30 minutes. The relaxation of anal sphincter and jaws was first to be noticed. Mild salivation was observed in only two animals. No lacrimation was observed in any of the animal in the study. Medetomidine hydrochloride produced mild to moderate depression of corneal reflex between 15 to 45 minutes interval. The palpebral reflex was not depressed following medetomidine administration in all the animals. There was complete depression of swallowing reflex in three animals between 5-30 minutes whereas in one animal, it remained

moderately depressed up to 75 minute intervals. Micturition was a constant feature during or after recovery. Rectal temperature and respiration rate, following administration of medetomidine hydrochloride did not alter significantly however, heart rate was significantly reduced throughout the period of study. Haematological parameters viz. haemoglobin, packed cell volume, total leukocyte count and total erythrocyte count were not affected during the period of study. A significant hyperglycemia was observed following medetomidine administration. Other biochemical parameters (total protein, blood urea nitrogen, total proteins, creatinine, aspartate aminotransferase, alanine aminotransferase, sodium, potassium and chloride) showed non-significant alteration precluding the sign of hepatic and renal toxicity. Medetomidine hydrochloride in neonatal calves produced highly significant bradycardia and highly significant decrease in systolic pressure, diastolic pressure and mean arterial pressure. Electrocardiographic studies revealed highly significant increase in QT-interval keeping the changes in other duration and conduction parameters statistically non-significant. Electroencephalographic studies revealed reduced electrical activity of brain indicating profound sleep.

Evaluation of chloral hydrate:

Chloral hydrate was evaluated in 5 neonate male calves. The dose rate computed for neonatal cow calves was 7.5 gm/100 kg bw, 4% solution, given by I/V route. The time of injection was 1.80 $\pm$ 0.27 minutes. Onset of effect was seen within 2-5 minutes with peak effect remaining for 17-25 minutes and sedation for 65-75 minutes. Complete relaxation was observed for 15 minutes with mild to moderate analgesia persisting up to 30 minutes. Chloral hydrate induced significant hypothermia, tachycardia and Tachypnea. There was a nonsignificant increase in haemoglobin and PCV values. No significant changes were observed in various times and voltage attributes of ECG. Elevation of ST segment was a constant feature in all the animals following chloral hydrate administration. Transient SA block was observed in one animal. Most of the biochemical parameters did not reveal any significant change in this group. However there was significant hyperglycemia with an increase in BUN levels. A wide variation was noticed in LDH behaviour in different

animals. Plasma levels of sodium, potassium, chloride, creatinine, total proteins, AST and ALT were not altered.

Evaluation of chloral hydrate + magnesium sulfate:

Chloral hydrate + magnesium sulfate was evaluated in 5 neonate male calves, 10-15 days old and weighing 20-27 kg. The neonatal calves of this group received a combination of chloral hydrate and magnesium sulfate (Chloral-mag) in 1:1 ratio as 6% solution. The dose rate used was 10 gm/100 kg body weight by intravenous route. The time of injection was 30-80 seconds (Mean 49). The onset of effect was observed between 2-7 min. Chloral-mag combination resulted in a peak effect of 8-39 minutes in neonatal calves with sedation remaining for 45-60 minutes. There was good muscle relaxation but without analgesia. There was gradual but significant decrease in the rectal temperature with a non-significant tachycardia in general. The respiratory rate remained with in the normal range but a significant fall was noticed at 45 min. interval only. No significant changes were observed in haemoglobin and PCV values following chloral-mag administration in neonatal cow calves. The time and voltage parameters of ECG were not affected. In this group also ST segment elevation was a constant feature in all the animals. The chloral-mag administration resulted in a gradual and significant increase in glucose levels of neonatal calves with a terminal hyperkalaemia. No significant variations were noticed in plasma levels of total proteins, sodium, chloride, BUN, creatinine, AST, ALT and LDH.

Evaluation of chloral hydrate + magnesium sulfate + thiopentone:

Chloral hydrate + magnesium sulfate and thiopentone sodium was evaluated in 5 neonate male calves, 10-15 days old and weighing 16-24 kg. Chloral-mag (1:1) was administered at the dose rate of 10 gm/100 kg body weight as 6% solution. Thiopental sodium (5%) was given 10 minutes later at a dose rate of 15 mg/kg body weight, ‘to effect’. Both the anaesthetics were infused by intravenous route. A combination of chloral-mag followed 10 min. later by thiopentone sodium induced surgical anaesthesia in neonatal calves. A dose of 100-150 mg. of thiopentone sodium was required to maintain anaesthesia in four animals. The peak effect was noticed for 60 min. or more with sedation remaining for 4 hours or more.

Breath holding was a common feature in all the animals. Relaxation and analgesia was noticed throughout the period of study. There was scanty salivation and lacrimation in one animal. A significant hypothermia with non significant tachycardia was observed following chloral-mag-thiopentone anaesthesia in neonatal cow calves with no effect on the respiration rate. The haemoglobin and haematocrit values were not affected. ECG studies revealed a slight increase in QoT, QT, T and ST segment intervals. Elevation of ST segment was a constant feature. Though non-significant, Chloral-mag thiopentone combination resulted in hyperglycaemia with an increase in AST and ALT values in neonatal calves. The other biochemical attributes viz. total proteins; sodium, potassium, chloride, BUN, creatinine and LDH were not affected.

Evaluation of xylazine hydrochloride + ketamine hydrochloride:

Xylazine + ketamine combination was evaluated in 5 neonate male calves, 10-15 days old and weighing 17-23 kg. Ketamine hydrochloride was used at the dose rate of 5 mg/kg body weight in the present study. It was given in combination with xylazine (0.22 mg/kg body weight) since there was a big problem of cataleptic effect when ketamine was used alone in the pilot trials (4 animals). Both the anaesthetics were given simultaneously, in single syringe, by intramuscular route. Surgical anaesthesia was induced with in 1-5 min with peak effect remaining for 23-47 min. However the animals remained deeply sedated for more than 60 min. Transient cataleptic effects were observed in two animals. Muscle relaxation and analgesia were observed for 45 min with scanty salivation in all the animals. There was a significant hypothermia and bradycardia with a significant increase in the respiratory rate. A slight but non significant decrease in haemoglobin and haematocrit values was recorded. ECG studies revealed a significant increase in PR, QoT, QT and ST segment intervals. Slight ST segment elevation with bifid P wave was observed in two animals. There was highly significant hyperglycaemia with significant fall in ALT concentrations. The other biochemical attributes remained with in normal range.

Evaluation of detomidine hydrochloride + ketamine hydrochloride:

Effects of detomidine hydrochloride + ketamine hydrochloride, intramuscularly, were evaluated in 15 male neonatal calves, 10 – 15 days old. The

doses of detomidine (0.02 mg/kg) plus ketamine (7.5 mg/kg) were standardized on subjective analysis. In neonate calves, surgical anaesthesia was induced within 5.6 ± 0.80 min following intramuscular administration of detomidine-ketamine as a single mixture. The peak effect remained for 28-75 min. The muscle relaxation was complete upto 45 min whereas complete analgesia persisted upto 30 min interval. One animal showed complete analgesia and muscle relaxation upto 75 min interval. The ocular and swallowing reflexes were absent till 45 min interval. There was initial lacrimation in one animal. Significant to highly significant bradycardia and hypothermia were observed throughout the period of study with significant increase in respiration rate at 5, 15 and 30 min interval only. Haematological parameters were not affected following detomidine-ketamine administration in neonate calves. There was evidence of increase in blood pressure upto 45 min in comparison to base value but the increase was non significant. ECG studies revealed significant to highly significant increase in PR-interval at 15, 60 and 75 min intervals. An increase in QRS amplitude and decrease in T-wave amplitude was recorded 5 min onwards till 75 min. Biphasic T-wave was noticed in one animal only. Following detomidine-ketamine anaesthesia, EEG revealed surgical state of anaesthesia in all the animals showing high voltage activity against the background of low voltage in comparison to the base value i.e. low voltage high frequency activity. A significant to highly significant hyperglycaemia upto 75 min interval and significant decrease in ALT at 15 min interval were noticed in the present study. There was non-significant increase in AST concentration at later stages of anaesthesia. Other biochemical attributes were not affected in the present study.

Evaluation of atropine sulfate + medetomidine hydrochloride and ketamine hydrochloride:

Seven calves were used during the pilot trials to standardize the dose of medetomidine hydrochloride and ketamine hydrochloride for I/M use as a single injection. On subjective analysis, based on the extent of sedation, muscle relaxation, analgesia produced and smooth recovery the dose rates of medetomidine and ketamine standardized were, 0.015 mg/kg and 10.00 mg/kg body weight, respectively. After computation of dose the remaining 12 animals were divided into two groups (Group 1 and Group 2) of 6 animals each. Surgical anaesthesia was induced within 4.5 $\pm$ 0.50 min following medetomidine + ketamine administration. The peak effect remained for 28 to 45 min. Winking of eyes, flapping of ears 15-18 min after medetomidine + ketamine administration and head shaking was observed in all the animals. There was complete loss of corneal reflexes upto 45 min interval in three animals whereas in other three animals mild to moderate depression was observed through out the period of study. Complete muscle relaxation was observed upto 45 min interval following medetomidine - ketamine administration. In five animals analgesia persisted uptill 45 min interval whereas in one animal it was moderate to complete to 60 min interval. There was complete depression of swallowing reflex upto 45 min in all the animals. Lacrimation and salivation were absent in all the animals. Following medetomidine + ketamine administration in neonate calves there was no significant change in rectal temperature and heart rate at different intervals of time. However, increase in respiratory rate was highly significant at 5, 15, and 30 min interval. All the haematological parameters remained within normal range in the present study.

Highly significant hyperglycemia was observed 15 min onwards till 75 min. A nonsignificant increase in BUN was noticed upto 75 min post administration of medetomidine + ketamine. Other biochemical attributes viz. ALT, AST, total proteins, creatinine, chloride, sodium and potassium were not affected in the present study.

There was initial rise of blood pressure after the administration of atropine and thereafter significant to highly significant hypotension was recorded following the injection of the anaesthetic combination of medetomidine + ketamine. There was an overall increase in different time interval parameters of ECG. The P-interval showed a gradual

decrease through out the period of study, whereas P-wave showed a slight and gradual increase.The QRS-complex increased intermittently till 75 min time interval. The T-wave showed a decrease in amplitude but it was statistically non-significant. There was ST-segment elevation and biphasic T-wave observed in all the animals. One animal showed atrial flutter at 75 min interval. EEG studies revealed low voltage high frequency waves changing to low voltage low frequency waves with burst suppressions indicating surgical state of anaesthesia.

Evaluation of diazepam plus thiopentone anaesthesia:

The present study was conducted on 12 clinically healthy male neonatal cow calves 10 to 15 days of age, weighing 18 to 28 Kg. 12 calves. These 12 calves divided randomly into two groups of six animals each (group I and group II) were used in the present study. After intravenous injection of diazepam (0.3 mg/Kg) there was onset of ataxia followed by lowering of the head. Mild relaxation of anal sphincters and tail was observed in all the animals. The onset time recorded was 1.11 $\pm$ 0.26 minutes. The down time recorded for lateral recumbency was 1.55 $\pm$ 0.33 minutes. The duration of analgesia recorded after diazepam-thiopentone anaesthesia was 10 to 15 minutes (15.5 $\pm$ 0.76 minutes) in all the calves. The sedation following diazepam-thiopentone anaesthesia remained for 2 to 3 hours (154.68 $\pm$ 4.59 minutes) in all the animals. However, neonatal calves took 6 to 7 hours (411 $\pm$ 15.96 minutes) for complete recovery from the effect of diazepam-thiopentone anaesthesia. The mean dose of thiopentone (I/V) “to effect” was found to be 10.2 $\pm$ 0.25 mg/Kg (9.72 to 11.0 mg/Kg). There was complete abolition of corneal, palpebral; photopupillary and swallowing reflex and it remained upto 30 minutes in all the neonatal calves following thiopentone administration. Complete relaxation of neck, tail, anal sphincter and jaws was observed at 5 minutes after administration of thiopentone. Diazepam-thiopentone anaesthesia did not produce lacrimation, defecation and urination in any of the neonatal calf during entire period of observations. Mild cough reflex and intermittent twitching of ear was noticed in two animals after intravenous administration of diazepam-thiopentone anaesthesia. Slight hypothermia was noticed at 45 to 75 minutes following thiopentone administration. Tachycardia was seen 10 minutes after diazepam administration and was remained

upto 75 minutes following thiopentone administration. Mild rise in respiratory rate was observed 10 minutes after diazepam administration and was remained upto 75 minutes following thiopentone administration. No appreciable change was recorded in Hb values during entire period of observations. Marginal increase in TEC and PCV was seen at 5 minutes and was remained upto 60 and 75 minutes respectively following thiopentone administration in all the calves. Slight decrease in TLC was observed at 10 minutes after diazepam administration. A non-significant hyperglycaemia was noticed at 5 minutes and remained upto 75 minutes after administration of thiopentone in all the neonatal calves. There was no appreciable change in plasma total proteins and creatinine values during entire period of observations following diazepam-thiopentone anaesthesia. The BUN concentration was decreased at terminal recordings in all the calves after administration of diazepam-thiopentone. No significant alterations were observed in serum enzyme (ALT & AST) and plasma electrolyte (Na, K & Cl) values. The diazepam (0.3 mg/Kg, I/V) produced mild but transient hypotension which remained upto 75 minutes following thiopentone administration in all the neonatal calves. There was no significant change observed in mean arterial pressure and pulse pressure. There were no clinical significant changes in ECG time and voltage components recorded after diazepam-thiopentone anaesthesia except some primary T-wave changes which include biphasic T-wave and inversion of T-wave. Biphasic T-wave was observed in all the calves. Electroencephalographic (EEG) changes revealed decrease in electrical activity of brain after diazepam-thiopentone anaesthesia and change of LVHF waves to LVLF waves with intermittent HVLF waves. Diazepam-thiopentone anaesthesia in the present series proved fatal in one animal and also did not indicate the safety of the combination (diazepam-thiopentone) in neonatal calves as the most neonates showed prolonged post anaesthetic recovery (6 to 7 hours).

Some of the parameters/objectives mentioned in the scheme could not be evaluated because of the following reasons:

1. The acid base and blood gas monitoring following drug(s) administration could not be carried out because of the non availability of the facilities.

2. The studies on the use of inhalant anaesthetics in neonate calves could not be carried out because of the break down of large animal anaesthetic machine.

Conclusions:

1. The effects following Atropine sulfate or Acepromazine maleate administration were quite variable.
2. Out of the preanaesthetics/sedative/tranquillizer studied, Detomidine hydrochloride (@ 0.02 mg/kg, I/M), xylazine hydrochloride (@ 0.22 mg/kg, I/M), Diazepam (@ 0.3 mg/kg, I/V) and Medetomidine hydrochloride (@ 0.01 mg/kg, I/M) proved as best pre-anaesthetics (sedatives/tranquillizer) for the neonatal calves.
3. Xylazine + ketamine, Detomidine + ketamine and Atropine + medetomidine + ketamine combinations produced excellent and balanced surgical anaesthesia in neonate calves and are recommended for safe clinical use by the veterinarians in neonate calves.
4. Significant to highly significant hyperglycaemia and hypotension were noticed in most of the groups.
5. There was no indication of liver or kidney damage in any of the groups studied under report.
6. The combinations of Chloral hydrate-magnesium sulfate-thiopentone and Atropine-diazepam-thiopentone did produce general anaesthesia in bovine neonate calves but their use in clinical cases for balanced surgical anaesthesia is questionable due to prolong recovery time.

Acknowledgements:

The financial assistant provide by ICAR, New Delhi is gratefully acknowledged. The physical facilities provided by CSK HPKV, Palampur are also thankfully acknowledged. The investigators are also thankful to all the faculty members, namely Dr. MS Kanwar, Dr. Adarsh Kumar and Dr. SP Tyagi, technical and non teaching staff and the post graduate students of the Department of Veterinary Surgery and Radiology, College of Veterinary and Animal Sciences, CSK HP Agril. University, Palampur, who directly or indirectly helped in the completion of

this project. A very special thank to Dean and Dr YP Thakur, Scientist Incharge of Livestock Farm, College of Veterinary and Animal Sciences, CSK HP Agril. University, Palampur who readily provided the neonate male calves to carry out the requisite work.

Signatures

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II. Dr. AC Varshney — Professor & Head

III. Dr. RC Thakur — Director of Research

16. Comments of the Referee:

17. Remarks of the council: