Haryana Vet. (Dec., 2015) **54 (2)**, 192-195

Research Article

EFFECT OF CHLORPROMAZINE AND KETAMINE ANAESTHESIA IN BUFFALO CALVES

CHANDER VIJAY PAL[1], ASHOK KUMAR[1]*, SANDEEP KUMAR[2], SANDEEP POTLIYA[1] and SUKHBIR SINGH[1]

[1]Department of Veterinary Surgery and Radiology
[2]Department of Veterinary Physiology and Biochemistry, College of Veterinary Sciences
Lala Lajpat Rai University of Veterinary and Animal Sciences, Hisar-125004, India

Received: 18.03.2015; Accepted: 09.11.2015

ABSTRACT

A study was conducted to evaluate the chlorpromazine-ketamine as an anaesthetic combination in six clinically healthy male buffalo calves by administering chlorpromazine (2.5 mg/kg, i.m.) and ketamine (2.0 mg/kg, i.v.). All the animals showed decreased spontaneous motor activity with ataxia after chlorpromazine administration. A transient apnoea was observed in two animals after ketamine administration. Auditory and swallowing reflexes were lost but palpebral reflex was present after ketamine injection. Muzzle became dry and analgesia was observed at fetlock joint of all the limbs, and on abdomen, base of horn and tail, and ribs after ketamine injection. Recovery was manifested by regaining of head righting reflex. Heart rate and sodium levels increased significantly at 5 min of ketamine administration. There was a significant decrease in respiratory rate during anaesthesia and at recovery. A non-significant decrease in haemoglobin and packed cell volume was observed at recovery. Plasma glucose level showed a non-significant increase during and after anaesthesia. Serum alanine transaminase activity increased non-significantly at 15 min of chlorpromazine administration while serum aspartate transaminase increased non-significantly at 15 min of chlorpromazine and at 5 min of ketamine administration.

Key words: Buffalo calves, chlorpromazine, ketamine

Phenothiazines provide good muscle relaxation and are often used in conjunction with anaesthetics that do not provide muscle relaxation or that result in muscle rigidity (Riviere and Papich, 2009). Chlorpromazine is considered as the prototype of the phenothiazine derivatives and is primarily used as an antiemetic in dogs and cats, but it is also used as preanaesthetic. Phenothiazine derivatives block alpha$_1$-adrenergic receptors, resulting in peripheral vasodilation producing arterial hypotension (Riviere and Papich, 2009). Ketamine is a dissociative anaesthetic agent, with a shorter duration of action. It is a potent respiratory depressant and induce apnoea in buffalo calves. Ketamine produce the hypertensive effects in calves but can be nullified by prior administration of diazepam (Singh *et al*., 1991). Midazolam-ketamine combination was found to be safe for general anaesthesia in buffalo calves with minimum cardiopulmonary and biochemical changes (Kumar *et al.,* 2014). A comprehensive and planned study on the effects chlorpromazine in combination with ketamine has not been done in buffaloes. Therefore, the present study was undertaken with the objective to evaluate efficacy and safety of chlorpromazine-ketamine anaesthesia in buffalo calves.

*Corresponding author: professorashokkumar@gmail.com

MATERIALS AND METHODS

The study was performed after taking prior permission from Institutional Animal Ethics Committee of the University on six clinically healthy male buffalo calves of 18 to 24 m of age and weighing 190-280 kg. Chlorpromazine (2.5 mg/kg) was administered intramuscularly (i.m.) and ketamine (2.0 mg/kg) was administered intravenously (i.v.) at 15 min of chlorpromazine administration. The parameters that were observed in the study included behavioural changes, rectal temperature, heart rate, respiratory rate, haemoglobin (Hb), packed cell volume (PCV), plasma glucose, urea nitrogen, creatinine, total plasma proteins, albumin, sodium, potassium, chloride, alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALKP), gamma glutamyl transpeptidase (GGT) and bilirubin. Blood samples were collected from jugular venipuncture before administration of the drug(s), at 15 min of administration of chlorpromazine, at 5 min of ketamine, at recovery and at 24 h of chlorpromazine administration. Plasma glucose, urea nitrogen,

creatinine, total plasma proteins, albumin, ALT, AST, ALKP, GGT and bilirubin were estimated by fully automatic biochemistry analyzer EM 200 (Erba Mannheim, Germany) using commercially available kits by M/S Transasia Biomedical Limited, Mumbai. Chloride was measured by colorimetric method by using kit procured from Bayer Diagnostic India Limited. Sodium and potassium were estimated by flame photometry method. The statistical analysis of data was done by one-way-analysis of variance and Duncan's multiple range test (Duncan, 1955).

RESULTS AND DISCUSSION

The effects of chlorpromazine-ketamine combination on behavioural parameters are shown in Table 1. All the animals showed decreased spontaneous motor activity with ataxia after chlorpromazine administration. All the animals remained standing calm and quiet. All phenothiazines decrease spontaneous motor activity in animals and exert a sedative action by depressing the brain stem and connection to the cerebral cortex (Riviere and Papich, 2009). Watery salivation was seen in two animals after chlorpromazine administration and it might be due to temporary para-sympathetic excitation (Lakshmipathy and Vijayakumar, 1980). Prepuce was seen relaxed after chlorpromazine injection only in one animal. Transient apnoea was observed in two animals for 4 and 5 sec, but the animals regained respiration without any resuscitation. When other CNS depressants are administered with ketamine, significant respiratory depression can be seen (Riviere and Papich, 2009). Palpebral reflex was present in all animals. The patient may not look asleep; N-Methyl-D-aspartate (NMDA) antagonists are effective in producing amnesia (Hass and Harper, 1992). Animals under anaesthesia showed intact palpebral and corneal reflexes; this observation is in contrary to the findings in goats by i.v. administration of midazolam-ketamine (Singh, 2004) and acepromazine-ketamine (Kumar and Thurmon, 1977). Analgesia was observed on abdomen, base of horn, tail, ribs and fetlock joint of all the limbs after ketamine injection. The analgesia might be mediated by the antagonistic effects of ketamine on NMDA receptor (Kohrs and Durieux, 1998). The NMDA receptor is also involved in pain processing, including central and peripheral sensitization and visceral pain (Riviere and Papich, 2009). Complete analgesia at fetlock, base of tail, abdomen, ribs periosteum and base of horn had been reported in buffalo calves after ketamine anaesthesia (Kumar *et al.*, 2014). Sarma and Kumar (1998) observed surgical anaesthesia of 33.75±3.12 min in crossbred male cow calves and Kumar *et al.* (1990) reported surgical anaesthesia of 38.25±5.32 min in dogs after atropine-diazepam-ketamine anaesthesia. Recovery was evident by movement of limbs with regain of muscle tone, regain of head righting reflex, return to sternal recumbency and complete recovery. Two animals showed praying posture on standing at recovery from anaesthesia. All the animals stood up, but still ataxic, at 16.17±0.94 min and complete recovery took 30.83±1.25 min of ketamine administration.

Table 1
Different behavioural characteristics affected by administration of chlorpromazine-ketamine combination in buffalo calves

Reflexes		Min(Mean±S.E.)
Spontaneous motor activity decrease*		7.00±0.52
Weak time*		9.83±0.60
Salivation*		2.50±1.82
Muzzle dryness†		2.00±0.26
Ventral rotation of Eye ball †		1.00±0.00
Relaxation of muscle	limbs†	1.83±0.31
Auditory reflex	Loss†	1.00±0.00
	Regain†	11.33±0.61
Swallowing reflex	Loss†	1.00±0.00
	Regain†	10.67±0.67
Onset of analgesia	Fetlock†	1.17±0.17
	Abdomen†	1.00±0.00
	Base of horn†	1.00±0.00
	Base of tail†	1.00±0.00
	Ribs†	1.00±0.00
Regaining of muscle tone†		11.67±0.71
Regaining of head righting reflex†		11.33±0.61
Return to sternal recumbency†		13.17±0.70
Standing with ataxia†		16.17±0.94
Complete recovery†		30.83±1.25

* minutes of chlorpromazine administration
† minutes of ketamine administration

The heart rate increased significantly at 5 min of ketamine administration as compared to the base value (Table 2). Increased heart rate may be due to cardiovascular stimulant property of ketamine, which is due to action on sympathetic trunk and inhibition of neuronal uptake of catecholamine by sympathetic nerve endings (Tweed *et al.*, 1972; Ivankovitch *et al.,* 1974) or may be due to increase in central release of catecholamine resulting in tachycardia (Hardie and Lukasik, 2007). Kumar *et al.* (1990) also reported increased heart rate after ketamine administration in dogs. There was a significant decrease in respiratory rate at 15 min of chlorpromazine administration which remained lower up to the recovery as compared to the base value (Table 2). Clinical doses of phenothiazine have little effect on respiratory activity. Respiratory rate

Table 2

Mean values (±standard error) of rectal temperature, heart rate, respiratory rate and haematological parameters in buffalo calves under chlorpromazine-ketamine anaesthesia

Parameters (Units)	Before administration of chlorpromazine	At 15 min of chlorpromazine administration	At 5 min of ketamine administration	At recovery	At 24 h of chlorpromazine administration
Ambient temperature (^{0}C)	32.17^a±0.74	32.17^a±0.74	32.33^a±0.67	32.33^a±0.67	32.33^a±0.80
Rectal temperature (^{0}C)	37.20^a±0.16	37.37^a±0.15	37.38^a±0.17	37.33^a±0.15	37.22^a±0.12
Heart rate (beats/min)	48.67^a±1.98	45.33^a±2.17	69.17^b±1.72	50.67^a±2.67	49.67^a±2.26
Respiratory rate (breaths/min)	20.00^c±1.03	15.67^b±0.95	12.17^a±0.54	15.00^b±0.81	19.17^c±1.24
Haemoglobin (g/dl)	9.37^a±0.36	9.57^a±0.36	9.50^a±0.43	8.53^a±0.24	9.37^a±0.35
Packed cell volume (%)	28.92^b±0.71	29.47^b±0.99	29.08^b±0.91	26.12^a±0.61	28.68^b±1.00

Means with different superscripts in a row vary significantly ($p<0.05$)

is often depressed but minute volume remains normal (Riviere and Papich, 2009). A non-significant decrease in Hb and a significant decrease in PCV was observed at recovery as compared to the base value (Table 2). Phenothiazines markedly reduce the haematocrit in animals due to the sequestration of red blood cells in spleen (Proakis and Borowitz, 1974). This decrease in Hb and PCV could be attributed to spleenic pooling of blood constituents (Welberg *et al.,* 2006).

The effects of chlorpromazine-ketamine combination on biochemical parameters are presented in Table 3. Plasma glucose level showed a non-significant increase during and after anaesthesia. The hyperglycaemia may be due to release of catecholamine in a stressful condition during anaesthesia resulted in glycogenolysis (Tammisto *et al*., 1982) or it may be due to decreased glucose utilization, impaired insulin activity or increased adrenocortical hormone (Kumar *et al*., 1989). Moreover, during the period of anaesthesia, there is a decrease in basal metabolic rate of the animal and muscular activity is negligible, so utilization of glucose by muscles is also decreased probably causing slight increase in glucose concentration. Since hyperglycaemia produced was transient in nature and within the normal physiological limits, so a clinical significance cannot be attached. Sodium increased significantly at 5 min of ketamine administration which became non-significantly higher at recovery as compared to the base value. The increase in sodium level may be the result of withholding feed and water or excess of mineralocorticoids (Carlson, 1997). The variations in concentrations of serum sodium, potassium and chloride were within the normal physiological limits. Singh *et al.* (1985) did not find any significant change in the plasma concentration of electrolytes after administration of xylazine-ketamine in buffalo calves. It can, therefore, be concluded that the blood dilution has not been caused by water or electrolyte retention, but most probably by the increased temporary migration of interstitial fluid to the

Table 3

Mean values (±standard error) of blood biochemical parameters in buffalo calves under chlorpromazine-ketamine anaesthesia

Parameters (units)	Before administration of chlorpromazine	At 15 min of chlorpromazine administration	At 5 min of ketamine administration	At recovery	At 24 h of chlorpromazine administration
Plasma glucose (mg/dl)	71.67^a±0.56	78.17^a±3.02	72.67^a±4.34	76.67^a±5.37	75.00^a±0.96
BUN (mg/dl)	15.21^a±0.79	16.28^a±1.53	15.72^a±1.20	16.92^a±1.22	15.72^a±0.95
Creatinine (mg/dl)	1.72^a±0.13	1.49^a±0.21	1.67^a±0.12	1.58^a±0.28	1.72^a±0.13
Total plasma proteins (g/dl)	6.20^a±0.20	5.98^a±0.21	6.12^a±0.26	6.12^a±0.24	6.02^a±0.20
Albumin (g/dl)	2.35^a±0.12	2.35^a±0.12	2.31^a±0.10	2.25^a±0.12	2.32^a±0.19
Sodium (mmol/L)	143.75^{ab}±1.30	139.77^b±2.89	155.08^c±1.54	147.57^b±2.42	146.22^b±1.22
Potassium (mmol/L)	6.26^a±0.37	6.16^a±0.35	5.96^a±0.49	5.58^a±0.48	6.32^a±0.38
Chloride (mmol/L)	84.08^a±3.05	85.52^a±4.69	95.26^a±3.78	86.17^a±5.74	95.16^a±1.34
ALT (IU/L)	56.03^{ab}±3.03	63.05^b±2.16	58.70^{ab}±3.07	57.22^{ab}±0.32	52.57^a±2.91
AST (IU/L)	109.20^{ab}±3.96	149.08^b±26.56	115.30^{ab}±7.20	112.01^{ab}±4.65	105.22^a±4.73
ALP (IU/L)	79.68^a±9.65	82.97^a±9.00	65.08^a±6.74	63.52^a±6.68	64.28^a±6.22
GGT (IU/L)	10.35^a±1.28	11.68^a±1.39	11.28^a±1.16	11.23^a±1.09	11.88^a±0.91
Bilirubin (mg/dl)	0.06^a±0.01	0.04^a±0.01	0.06^a±0.02	0.06^a±0.02	0.05^a±0.01

Means with different superscripts in a row for a parameter vary significantly ($p<0.05$)

vascular system.

The ALT and AST activities increased non-significantly during anaesthesia and it may be due to increased permeability of these enzymes through plasma membrane of hepatic cells in anaesthetized animals (Vickers *et al.*, 1984). A significant rise in ALT value was reported by Pandey and Sharma (1994) in canine after diazepam-ketamine anaesthesia. Elevated AST and ALT values were also reported by Kumar *et al.* (1989) during maximal depth of anaesthesia in dogs. Other biochemical parameters showed non-significant variation within normal limits. Based on these observations, it can, therefore, be concluded that combination of chlorpromazine-ketamine may safely be used in buffalo calves.

REFERENCES

Carlson, G.P. (1997). Fluid, Electrolyte and Acid-Base Balance. In: Clinical Biochemistry of Domestic Animals. (5th edn.) Academic Press, San Diego, USA.

Duncan, D.B. (1955). Multiple range test and multiple 'F' tests. *Biometrics*. **11:** 1-42.

Hardie, E.M. and Lukasik, V.M. (2007). Orthopedic patients. In: Veterinary Anesthesia and Analgesia (Lumb and Jones, edts.) (4thedn.), Blackwell Publishing, Oxford.

Haskin, S.C., Farver, T.B. and Partz, J.D. (1986). Cardiovascular changes in dogs given diazepam and diazepam-ketamine. *American J. Vet. Res.* **47:** 636-641.

Hass, D.A. and Harper, D.G. (1992). Ketamine: A review of its pharmacologic properties and use in ambulatory anesthesia. *Anesth. Prog.* **39:** 61-8.

Ivankovitch, A.D., Melietch, D.J., Reinmnn, C., Albrecht, R.F. and Zahed, B. (1974). Cardiovascular effects of centrally administered ketamine in goats. *Anesth. Analg.* **53:** 924-923.

Kohrs, R. and Durieux, M.E. (1998). Ketamine: Teaching an old drug new tricks. *Anesth. Analg.* **87:** 1186-1193.

Kumar, A. and Singh, H. (1977). Chlorpromazine hydrochloride, triflupromazine hydrochloride and xylazine as tranquilizers in buffaloes. *Indian Vet. J.* **54**: 984-988.

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

Kumar, A., Kumar, A., Singh, S. and Chaudhary, R.N. (2014). Evaluation of midazolam-ketamine as an anaesthetic combination in buffalo calves. *Haryana Vet.* **53(2):** 117-120.

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

Kumar, N., Kumar, A. and Singh, B. (1989). Haematological and biochemical effects of ketamine with or without meperidine and diazepam in dogs. *Indian J. Anim. Sci.* **59(7):** 815-818.

Kumar, N., Kumar, A. and Singh, B. (1990). Clinical and physiological effects of ketamine with or without diazepam or meperidine premedication in dogs. *Indian Vet. J.* **67:** 242-246.

Lakshmipathy, G.V. and Vijayakumar, D.S. (1980). Siquil sedation in buffalo calves (*Bos bubalis*) and its effects on rectal temperature, coccygeal pulse, heart rate, and respiration. *Indian Vet. J.* **57**: 211-214.

Pandey, S.K. and Sharma, I.J. (1994). Effect of diazepam-ketamine anaesthesia on liver and kidney functions in canine surgical patients. *Indian J. Anim. Sci.* **64(1):** 48-50.

Pathak, S.C., Nigam J.M., Peshin, P.K. and Singh, A.P. (1982). Anesthetic and hemodynamic effects of ketamine hydrochloride in buffalo calves. *American J. Vet. Res.* **43**: 875-878.

Proakis, A.G. and Borowitz, J.L. (1974). *Biochem. Pharmacol.* **23**: 1693. [Cited by Booth, N.H. 1988. Psychotropic agents. In: Veterinary Pharmacology and Therapeutics (Booth, N.H. and McDonald, L.E. eds). (6th edn.), Iowa State University Press. Iowa.].

Riviere, E.J. and Papich, M.G. (2009). Veterinary Pharmacology and Therapeutics. (9th edn.), Iowa State University Press, Ames.

Sarma, B. and Kumar, A. (1998). Clinical and cardiopulmonary effects of atropine-diazepam-ketamine with or without guaifensin in calves suffering from acute renal failure. *Indian J. Anim. Sci.* **68(9):** 901-903.

Singh, A.P., Singh, J., Peshin, P.K., Singh, P. and Nigam, J.M. (1985). Evaluation of xylazine-ketamine anaesthesia in buffaloes (*Bubalus bubalis*). *Zbl. Vet. Med.* A. **32:** 54-58.

Singh, K. (2004). Evaluation of ketamine as an anaesthetic in goats (*Capra hircus*) with midazolam premedication. MVSc thesis, CCS Haryana Agricultural University, Hisar, Haryana.

Singh, K.I., Sharma S.N., Mirakhur, K.K. and Singh, S. (1991). Haemodynamic and respiratory effects of diazepam-ketamine anaesthesia in calves. *Indian Vet. J***. 68**: 1157-1162.

Singh, S., Singh, K., Kumar, A. Singh, J., Singh, S. and Peshin, P.K. (2011). Evaluation of atropine-acepromazine-xylazine-ketamine combination for general anaesthesia in buffalo calves. *Indian J. Vet. Surg.* **32(2):** 99-102.

Tammisto, T., Jaateela, A., Nikki, P. and Takki, S. (1982). Effect of pentazocine and pethidine in plasma catecholamine level. *Anim. Clinical Res.* **3:** 22-29.

Tweed, W.A., Minuck, M. and Nymin, D. (1972). Circulatory response to ketamine anaesthesia. *Anesthesiol.* **37:** 613.

Vickers, M.D., Schnieden, H. and Wood, S.F.G. (1984). Drugs in Anaesthetic Practice. (6thedn.), Butterworths, London.

Welberg, L.A., Kinkead, B., Thrivikraman, K., Huerkamp, M.J., Nemeroff, C.B. and Plotsky, P.M. (2006). Ketamine-xylazine-acepromazine anesthesia and postoperative recovery in rats. *J. American Assoc. Lab. Anim. Sci.* **45**: 13-20.