Haryana Vet. (June, 2016) **55 (1)**, 53-55

Research Article

EVALUATION OF LORAZEPAM AS A SEDATIVE IN BUFFALO CALVES

AMRESH KUMAR, ASHOK KUMAR*, SUKHBIR SINGH and SANDEEP POTILYA
Department of Veterinary Surgery and Radiology, College of Veterinary Sciences,
Lala Lajpat Rai University of Veterinary and Animal Sciences, Hisar, Haryana- 125 004, India

Received: 30.09.2015; Accepted: 14.03.2016

ABSTRACT

The study was done in six clinically healthy male buffalo calves, 6 to 12 months of age, and weighing between 105 to 135 kg. Lorazepam (2.0 mg/kg) was administered intravenously in the jugular vein. All the animals went into sternal recumbency immediately after intravenous administration of lorazepam with drooping of lower lip at 0.45±0.06 min of its administration. The animals appeared sleepy with eyes completely closed at 7.61±0.55 min. All calves went into lateral recumbency at 0.83±0.18 min of lorazepam administration. There was complete relaxation of muscles. Swallowing reflex was abolished at 15.44±0.74 min of lorazepam administration and all the animals returned to sternal recumbency at 43.73±3.52 min. Complete recovery took 139.23±6.65 min. Heart and respiratory rate decreased significantly at 10 min of lorazepam administration. There was a significant increase in creatinine levels at 10 min of lorazepam administration as well as at recovery. A significant increase in activities of alanine amino transferase and aspartate amino transferase; and bilirubin content was observed at 10 min of lorazepam administration. Alkaline phosphatase activity showed a significant decrease at 10 min of lorazepam administration and at recovery.

Key words: Buffalo calves, lorazepam, sedative

Lorazepam is a high potency benzodiazepine drug which has all five intrinsic benzodiazepine effects: anxiolytic, amnestic, sedative/hypnotic, anticonvulsant and muscle relaxant. It may be useful as an antiepileptic therapy with IV administration in the dogs (Podell *et al*., 1998). Lorazepam (0.3 mg/kg IV and IM) in horse had been reported to increase rectal temperature, heart rate and respiratory rate and there was various degree of incoordination with a marked degree of ataxia of hind limbs (Fuenets *et al*., 2006). No appreciable change in cardiopulmonary system was observed in dogs after 5 min of lorazepam administration and it was concluded that lorazepam-thiopental sodium combination was found suitable for orthopedic surgery as muscle relaxation was adequate and reduction of fractured end was easier (Singh *et al*., 1989). Hence the study was planned with the objective to evaluate the efficacy and safety of lorazepam in buffalo calves.

MATERIALS AND METHODS

This study was done in accordance with prior approval of Institutional Animal Ethics Committee in six clinically healthy male buffalo calves, 6 to 12 months of age, and weighing between 105 to 135 kg. Lorazepam (2.0 mg/kg) was administered intravenously in the jugular vein. Various parameters were observed before administration of lorazepam, after 10 min of lorazepam administration, at recovery and at 24 h of recovery. The parameters were: Sedative effects, rectal temperature, heart rate, respiratory rate, haemoglobin (Hb), packed cell volume (PCV), plasma glucose, blood urea nitrogen (BUN), creatinine, total plasma proteins, albumin, inorganic phosphorus, calcium, magnesium, sodium, potassium, chloride, alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALKP) and bilirubin. The data was statistically analysed by one-way-analysis of variance (Duncan, 1955).

*Corresponding author: professorashokkumar@gmail.com

RESULTS AND DISCUSSION

The effects of administration of lorazepam on behavioural parameters in buffalo calves are shown in Table 1. All the animals went into sternal recumbency with drooping of lower lip immediately after intravenous administration of lorazepam. The animals appeared sleepy with eyes completely closed. Lorazepam has been reported to produce depression of spinal reflexes and these reflexes are modulated by the ascending reticular system in the brain stem. Like other drugs of benzodiazepine group, its action is also mediated by GABA receptor (Baldessarini, 2001). There was complete relaxation of muscles of tail, anus, prepuce, neck, limbs and tongue, no swallowing reflex and partially relaxed jaw muscles after lorazepam administration. Lorazepam affected polysynaptic reflexes in the spinal cord with very mild effect upon sensorial level related with the pharmacological effect of tranquilization and sedation (Baldessarini, 2001). Similar findings as observed in this study were reported in dogs by Singh *et al.* (1989). Recovery was manifested by opening of eye lids and movement of limbs with return of head raising reflex. All the animals returned to sternal recumbency remained in milk-fever posture. Animals started nibbling of grass and took 2-3 attempts to stand up and they stood up with hind limbs held apart with head down.

Table 1
Different behavioural characteristics induced by administration of lorazepam in buffalo calves

Reflexes		Mean time±S.E. (min)
Drooping of lower lip		0.45±0.06
Eyes closed		7.61±0.55
Onset of salivation		5.34±0.27
Assumption of lateral recumbency		0.83±0.18
Onset lacrimation		4.80±0.73
Loss of palpebral reflex		13.13±1.34
Relaxation of muscle	Prepuce	4.34±0.74
	Tail	8.48±1.85
	Neck	0.54±0.06
	Limbs	6.75±0.57
	Jaw	5.92±0.29
Swallowing reflex	Loss	15.44±0.74
	Regain	22.31±1.23
Regaining of muscle tone		32.34±2.14
Eyes open		25.61±0.84
Regaining of head rightening reflex		36.05±2.47
Return to sternal recumbency		43.73±3.52
Browsing time		61.17±5.79
Standing with ataxia		80.31±4.53
Complete recovery		139.23±6.65

Anaesthesia of 21.53±1.56 min with moderate sedation and incomplete muscle relaxation was reported by Singh and Sahay (1999) in atropinized goats after ketamine-lorazepam anaesthesia.

The effects of lorazepam on rectal temperature, heart and respiratory rates; and haemato-biochemical parameters are shown in Table 2. There were no significant variations in rectal temperature during the entire period of observation. Heart rate decreased significantly at 10 min of lorazepam administration and remained lower than base value up to recovery but returned to base value at 24 h of recovery. Decreased heart rate was observed by Singh and Sahay (1999) at different stages after atropine-ketamine-lorazepam anaesthesia in goats. Respiratory rate remained significantly lower after lorazepam administration in this study.

There were no significant variations in Hb and PCV during the entire period of observation. The non-significant decrease in Hb and PCV was reported in goats after pentazocine-lorazepam and pentazocine-lorazepam-atropine anaesthesia by Maji *et al.* (1992). The decrease in Hb and PCV might be attributed to the shifting of fluid from extravascular compartment to intravascular compartment in order to maintain normal cardiac output in animals (Wagner *et al.*, 1991). Pooling of circulating blood cells in the spleen and other reservoirs secondary to decreased sympathetic activity could be the reason for a decrease in Hb and PCV (Kilic, 2004; Pawde *et al.*, 2000).

A non-significant increase in glucose was observed during lorazepam anaesthesia, which became lower than base value at 24 h of recovery. There was a significant increase in creatinine at 10 min of lorazepam administration and at recovery in comparison to base value. Albumin level remained higher after lorazepam administration. A non-significant increase in calcium was observed at 10 min of lorazepam administration in comparison to base value Likewise a non-significant decrease in phosphorus level was also observed. There was non-significant decrease in sodium at 10 min. of lorazepam administration.

A significant increase in ALT activity was observed at 10 min of lorazepam administration. The ALT activity is particularly useful in measuring hepatic necrosis; it is only used in small animals and primates since liver of large species like horse, cattle and sheep contain only insignificant amount of ALT. The AST has been used rather than ALT in large animals, although it is not liver specific and its activity is also elevated in myocardial and skeletal muscle diseases (Cornelius, 1989). A significant increase in AST activity was observed at 10 min of lorazepam administration and at complete recovery and value remained higher at 24 h of recovery. Singh *et al.* (1999) reported significant rise in AST activity and non-significant rise in ALT activity after atropine-lorazepam-ketamine anaesthesia in goats. Both lorazepam and diazepam are the drugs of benzodiazepine group having almost similar chemical and physical properties. The increase in liver serum marker enzymes like AST and ALT is mainly due to their leakage from liver cytosol into the blood stream as a result of oxidative tissue damage induced by lorazepam, or diazepam (Abdelmajeed, 2009) or it may be due to increased permeability of these enzymes through plasma membrane of hepatic cells in anaesthetized animals due to oxidative transformation of these drugs in the liver during the process of elimination (Vicker *et al.*, 1984). Alkaline phosphatase showed significant decrease at 10 min of lorazepam administration and at recovery in comparison to base value. Serum ALKP was significantly decreased in buffalo calves after induction of anaesthesia with ketamine (Mottelib, 1980).

Total bilirubin was significantly higher at 10 min of lorazepam administration and at complete recovery in comparison to base value, while it reached nearer to base value at 24 h of recovery. Total bilirubin level in blood is an indicator of liver function as well as erythrocyte status of the body. Its level increases because of increased production (as in haemolysis), decreased clearance, inadequate conjugation, or impaired biliary excretion (Rothuizen, 2000). Elevated bilirubin levels in ruminants in haemolytic crisis (Cornelius, 1989) may explain the reason for increased bilirubin level, as the slight haemolysis was a constant finding in the plasma samples collected at 10 min of lorazepam administration and at complete recovery, while no haemolysis was observed in the plasma of base

Table 2
Effects of lorazepam administration on clinico-haemato-biochemical parameters in buffalo calves

Parameters (units)	Before administration of lorazepam	At 10 min of lorazepam administration	At recovery	At 24 h of recovery
Ambient temperature (ºC)	30.75^{a}±0.48	31.63^{ab}±0.45	33.75^{d}±0.28	31.63^{ab}±0.61
Rectal Temperature (ºC)	37.7^{a}±0.11	37.5^{a}±0.14	37.4^{a}±0.12	37.5^{a}±0.22
Heart Rate (beats/min)	61.8^{b}±0.79	51.5^{a}±1.15	57.8^{b}±1.93	61.5^{b}±1.47
Respiratory rate (per min)	15.3^{cd}±0.31	12.8^{ab}±1.29	14.5^{bcd}±0.56	14.0^{abc}±0.47
Haemoglobin (g/dl)	11.4^{a}±0.34	10.7^{a}±0.41	11.1^{a}±0.26	11.4^{a}±0.36
Packed cell volume (%)	26.8^{a}±0.83	26.0^{a}±0.79	26.0^{a}±0.70	27.0^{a}±0.79
Blood glucose (mg/dl)	59.25^{a}±3.83	65.50^{a}±3.90	66.25^{a}±4.12	56.25^{a}±3.53
BUN (mg/dl)	20.2^{a}±0.96	21.1^{a}±1.07	19.5^{a}±0.84	20.1^{a}±1.17
Creatinine (mg/dl)	2.2^{a}±0.09	2.6^{b}±0.12	2.6^{b}±0.15	2.1^{a}±0.07
Total proteins (g/dl)	7.20^{a}±0.38	7.85^{a}±0.30	7.77^{a}±0.24	7.14^{a}±0.36
Albumin (g/dl)	3.76^{ab}±0.19	4.22^{b}±0.12	4.19^{b}±0.15	3.50^{a}±0.27
Globulin (g/dl)	3.44^{a}±0.20	3.63^{a}±0.18	3.58^{a}±0.13	3.40^{a}±0.19
Albumin: globulin ratio	1.10^{ab}±0.02	1.08^{ab}±0.05	1.19^{b}±0.05	0.98^{a}±0.06
Calcium (mg/dl)	9.13^{ab}±0.20	11.05^{b}±0.52	9.98^{bc}±0.24	7.93^{a}±0.62
Phosphorus (mg/dl)	7.65^{b}±0.22	6.93^{ab}±0.41	7.10^{ab}±0.09	7.05^{b}±0.18
Magnesium (mEq/l)	4.48^{a}±0.21	4.39^{a}±0.12	4.43^{a}±0.23	4.37^{a}±0.30
Chloride (mEq/l)	96.58^{a}±1.31	98.23^{a}±2.67	101.13^{a}±1.12	96.58^{a}±3.78
Sodium (mmol/l)	129.05^{b}±1.08	125.65^{ab}±2.30	128.35^{b}±1.72	126.28^{ab}±1.60
Potassium (mmol/l)	5.10^{a}±0.12	5.13^{a}±0.12	4.97^{a}±0.19	5.00^{a}±0.23
ALT (U/L)	49.52^{a}±2.07	57.06^{b}±1.79	54.54^{ab}±1.80	50.06^{a}±1.91
AST(U/L)	175.20^{a}±2.42	187.93^{b}±4.08	188.30^{b}±2.81	183.68^{ab}±3.17
ALKP (U/L)	119.25^{b}±6.67	67.00^{a}±1.81	69.50^{a}±2.96	112.00^{b}±4.80
Bilirubin (mg/dl)	0.19^{a}±0.01	1.12^{c}±0.03	0.71^{b}±0.04	0.19^{a}±0.01

All values are mean±SE of six calves. Mean values with different superscripts vary significantly ($p<0.05$). BUN=Blood urea nitrogen; ALT=Alanine aminotransferase; AST=Aspartate aminotransferase; ALKP=Alkaline phosphatase

sample and at 24 h after recovery. There were no significant variations in other blood biochemical parameters studied. On the basis of these observations, it may be concluded that lorazepam may be used for short term (10-15 min) anaesthesia in buffalo calves.

REFERENCES

Abdelmajeed, N.A. (2009). Diazepam-induced oxidative stress in rat's different organ. *Res. J. Med. Medical Sci.* **4**: 295-302.

Baldessarini, R.J. (2001). Drugs and the Treatment of Psichyatric Disorders. In: Goodman and Gilman's; The Pharmacological Basis of Therapeutics. Hardman, J.G.; Limbird, L.T. and Gilman G.A. (edts.). (10th edn.). McGraw Hill Professional.

Cornelius, C.E. (1989). Liver Function. In: Clinical Biochemistry of Domestic Animals. (4th edn.). Academic Press, Inc. San Diego, California.

Duncan, D.B. (1955). Multiple range and multiple F test. *Biometrics.* **11**: 15-18.

Fuenets, V.O., Fuenets-Castro, M.L. and Fuenets-Castro, P.I. (2006). The effect of lorazepam on the horse. *J. Anim. Vet. Adv.* **5(10)**: 875-877.

Kilic, N. (2004). Physiological and haematobiochemincal changes in ketamine/diazepam anaesthesia in horse. *Indian Vet. J.* **81**: 396-398.

Maji, A. K., Deokiouliyar, U.K., Sahay, P.N. and Dass, L.L. (1992). Haematological alterations induced by pentazocine and lorazepam with and without atropine in goats. *Indian J. Anim. Hlth.* **31(2)**: 131-133.

Mottelib, A.A. (1980). Clinical and serum biochemical studies on the effect of ketamine in buffalo calves. *Zentralblatt für Veterinärmedizin Reihe A*. **27**: 596599.

Pawde, A.M., Amarpal, Kinjavdekar, P., Aithal, H.P., Pratap, K. and Bisht, G.S. (2000). Detomidine-diazepam-ketamine anaesthesia in buffalo (*Bubalus bubalis*) calves. *J. Vet. Med.* **47(3)**: 175-179.

Podell, M., Wgner, S.O. and Sams, R.A. (1998). Lorazepam concentrations in plasma following its intravenous and rectal administration in dogs. *J. Vet. Pharmacol. Therap.* **24**: 158-160.

Rothuizen, S. (2000). Jaundice. In: Text Book of Veterinary Internal Medicine. Ettinger, S.J. and Feldman, E.C. (edts.) (5th edn.). W. B. Saunders Company, Philadelphia, Pennyslyvania.

Singh, S.K. and Sahay, P.N. (1999). Clinico-anaesthetic effects of ketamine-lorazepam anaesthesia in atropinized goats. *J. Res. (Birsa Agricultural University).* **11(2)**: 251-253.

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

Singh, K., Sobti, V.K., Bansal, P.S. and Rathore, S.S. (1989). Studies on lorazepam as premedicant for thiopental anaesthesia in the dog. *J. Vet. Med. Series-A.* **36(10)**: 750-754.

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

Wagner, A.E., Muir, W.W. and Hinchcliff, K.W. (1991). Cardiovascular effects of xylazine and detomidine in horses. *American J. Vet. Res.* **52**: 651-657.