

HAEMATO-BIOCHEMICAL RESPONSE TO LUMBAR EPIDURAL ANAESTHESIA USING XYLAZINE, KETAMINE ALONE AND ITS COMBINATION IN BUFFALO CALVES

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ABSTRACT

Xylazine is very popular sedative, analgesic and muscle relaxant. Ketamine is widely used dissociative anaesthetic. The present communication gives an insight into the effect of xylazine, ketamine alone and their combination on haemato-biochemical parameters after lumbar epidural administration in buffalo calves.

Keywords: buffalo calves, ketamine, spinal epidural anaesthesia, xylazine

INTRODUCTION

Xylazine was introduced for veterinary use as a sedative, analgesic and muscle relaxant in late 1960's (Clarke and Hall, 1969; Kerr *et al.*, 1972). Epidural xylazine produces the local analgesic effect by inhibiting impulse conduction at adrenoceptors in the CNS and spinal cord. Xylazine is the most popular alpha-2 adrenoceptor agonist. Xylazine has been used for intraspinal (epidural or subarachnoid/intrathecal) administration for quite some time now but other alpha-2 agonists have been used for the purpose only in few experimental studies in the recent years. Reports regarding epidural use of xylazine and ketamine alone and its

combination in buffaloes are scanty. Ketamine hydrochloride is a congener of phencyclidine and chemically designated as (2-{0-chlorophenyl}-2-methylaminocyclohexanone). The commercial product is a 50:50 racemic mixture (Ryder *et al.*, 1978). The positive isomer is more potent than negative isomer for analgesic properties (White *et al.*, 1980). Ketamine rapidly crosses the blood brain barrier, quickly enters the brain and the brain/plasma concentration ratio becomes constant in less than one minute. The analgesic properties of ketamine may be mediated via blockade of high affinity monoaminergic uptake sites and inhibition of reuptake of neurotransmitters (Smith *et al.*, 1981). Therefore the present study was undertaken to study the effect of xylazine, ketamine alone and its in combination after lumbar epidural administration in buffalo calves.

MATERIALS AND METHODS

Non-descript, healthy male buffalo calves (5) ranging from 6 to 8 months of age and weighing from 55 to 75 kg were used in this study. The animals were stall fed, provided clean drinking water and kept under uniform management conditions throughout the period of observation. Each animal was kept off feed for 24 h and water was withheld for 12 h prior to start of experiment.

The animals were restrained in standing position and the lumbar region (between 1st and 2nd) space was prepared for aseptic injection of drug.

The animals were divided in 3 treatment groups A, B and C comprising 5 animals in each group. In group A, xylazine 0.1 mg/kg, group B ketamine 2.50 mg/kg body weight and in group C xylazine 0.1 mg/kg+ketamine 2.50 mg/kg body weight was injected epidurally in lumbar region. The total volume of the drug injected was made 4 ml in all the treatment groups after reconstituting them with distilled water for lumbar epidural injection.

Haematological parameters

Venous blood (1 ml) from external jugular vein was collected before and at 30, 60, 120, 240 minutes and 24 h interval after administration of drug in clean dry glass vials containing 2 mg of ethylene diamine tetra acetic acid. The various haematological parameters included estimation of haemoglobin, packed cell volume, total erythrocyte count and differential leucocyte count (Jain, 1986).

Biochemical parameters

Venous blood (8 to 10 ml) was collected in dry test tube before and at 60, 120, 240 minutes and 24 h interval following administration of drugs. Serum was separated for estimation of serum glucose, serum total protein, serum urea nitrogen, creatinine and aspartate aminotransferase levels using Computerized Semi-Automated Analyzer (ROBONIK-ASP 300).

The data obtained by using different combination of anaesthetic drugs were analysed as per Snedecor and Cochran (1967).

RESULTS AND DISCUSSION

Haematological parameters

A non-significant decrease in haemoglobin concentration in all the groups was observed (Table 1) between half an hour to 2 h of analgesia. The values ranged from 7.82 ± 0.05 gm/dl to 8.62 ± 0.05 gm/dl in different groups of animals at various intervals, which might have resulted from pooling of circulating blood cells in the spleen secondary to decreased sympathetic activity which was also observed in buffaloes (Sharda *et al.*, 2008). The decrease in haemoglobin during the period of anaesthesia might also be due to shifting of fluids from extravascular to intravascular compartment in order to maintain normal cardiac output in the animals (Wagner *et al.*, 1991).

Similarly non-significant decrease in packed cell volume (Table 1) between half an hour to 2 h was observed in all the treatment groups. The mean values ranged from 23.47 ± 0.07 percent to 26.29 ± 0.09 percent in different groups at various intervals. The decrease in packed-cell volume and total erythrocyte count during the period of anaesthesia might also be due to shifting of blood from extravascular compartment to intravascular compartment (Wagner *et al.*, 1991) to maintain normal cardiac output in animals. Non significant decrease was recorded in neutrophil count in all the groups (Table 1) between half and 2 h and the values had reached to near or above the base line within 24 h in all the groups. The mean values ranged from 32.20 ± 0.37 to 34.80 ± 0.09 percent in all the animals of three groups at various intervals. Pooling of the circulating blood cells in the spleen or other reservoirs secondary to decreased sympathetic activity could be the reason for decrease in Hb, PCV and TLC recorded in this study as also reported with other tranquillizers in dog (Soliman

Table 1. Effect on haematological parameters after lumbar epidural administration of Xylazine, Ketamine alone and their combination in buffalo calves.

Parameters	Groups	Time Interval (h)				
		0	½	1	2	24
Hb (gm/dl)	A	8.57±0.07	7.82±0.05	8.21±0.03	8.34±0.06	8.38±0.02
	B	8.62±0.05	8.11±0.02	8.34±0.01	8.41±0.09	8.58±0.04
	C	8.21±0.04	7.99±0.05	8.06±0.06	8.10±0.05	8.15±0.05
PCV (%)	A	24.66±0.16	23.75±0.17	23.47±0.07	24.14±0.04	24.50±0.08
	B	26.29±0.09	25.40±0.12	26.04±0.15	26.14±0.06	26.28±0.16
	C	24.39±0.04	24.00±0.02	24.12±0.06	24.20±0.06	24.31±0.02
TLC (x 10 ³ cumm ⁻¹)	A	4.88±0.01	4.29±0.03	4.15±0.02	4.09±0.03	4.77±0.03
	B	4.72±0.02	4.30±0.02	4.11±0.02	4.38±0.04	4.65±0.02
	C	4.34±0.01	3.97±0.01	3.87±0.01	3.99±0.01	4.27±0.03
I. Neutrophils	A	33.00±0.70	34.00±0.70	34.60±0.50	34.40±0.39	33.60±0.48
	B	32.20±0.37	33.60±0.67	34.40±0.58	34.20±0.37	34.40±0.58
	C	32.40±0.06	33.40±0.06	34.40±0.06	34.60±0.05	34.80±0.39
II. Lymphocytes	A	56.40±0.67	55.20±0.66	54.80±0.66	55.00±0.44	55.40±0.44
	B	57.40±0.67	57.00±0.54	56.00±0.83	56.60±0.97	56.20±0.81
	C	55.40±0.50	54.60±0.50	53.80±0.37	53.60±0.24	53.80±0.37
III. Monocytes	A	5.40±0.58	4.20±0.37	3.80±0.39	4.00±0.00	4.10±0.24
	B	6.00±0.31	4.80±0.37	4.40±0.24	4.20±0.31	4.20±0.19
	C	5.00±0.31	5.20±0.48	5.40±0.37	5.00±0.00	5.20±0.19
IV. Eosinophils	A	5.20±1.24	6.60±1.16	6.80±0.94	7.00±0.72	6.90±0.79
	B	4.40±0.50	4.60±0.97	5.20±1.28	5.00±0.86	5.20±1.07
	C	7.20±0.73	7.00±0.89	6.40±0.31	6.80±0.37	6.20±0.24
D						
L						
C						
(%)						

Table 2. Effect on biochemical parameters after lumbar epidural administration of Xylazine, Ketamine alone and their combination in buffalo calves.

Parameters	Groups	Time Interval (h)			
		0	1	2	24
Glucose (mg/dl)	A	60.40±0.92	73.20±1.19 ^{**a}	68.40±0.50 ^{**a}	62.20±0.79
	B	61.20±0.66	69.20±0.70 ^{**b}	65.00±0.54 ^{**b}	61.60±0.37
	C	61.80±0.66	76.20±0.66 ^{**ab}	82.20±0.86 ^{**ab}	62.40±0.70
Total Protein (mg/dl)	A	6.44±0.09	6.38±0.09	6.40±0.09	6.43±0.09
	B	6.61±0.01	6.46±0.01	6.52±0.01	6.56±0.01
	C	6.65±0.02	6.57±0.02	6.59±0.01	6.61±0.02
BUN (mg/dl)	A	6.03±0.06	6.59±0.02 ^{**a}	6.41±0.04 ^a	6.12±0.06
	B	6.04±0.04	6.19±0.03 ^{*b}	6.22±0.04 ^{**b}	6.09±0.04
	C	6.17±0.03	7.15±0.03 ^{**ab}	7.19±0.03 ^{**b}	6.31±0.04
Creatinine (mg/dl)	A	1.09±0.04	1.89±0.02 ^{**a}	1.91±0.02 ^{**a}	1.16±0.01
	B	1.08±0.01	1.29±0.01 ^{*a}	1.17±0.01 ^a	1.13±0.01
	C	1.19±0.01	1.64±0.01 ^{**b}	1.40±0.01 ^{**b}	1.20±0.02
AST (U/L)	A	21.60±0.39	23.60±0.39 ^{**a}	23.60±0.39 ^a	22.00±0.54
	B	24.60±0.50	25.60±0.50 ^b	24.60±0.50 ^a	24.20±0.39
	C	24.20±0.58	26.20±0.58 ^{**ab}	26.80±0.73 ^{**ab}	25.40±0.50

Means bearing different superscripts differ significantly at corresponding intervals (P<0.05)

*P<0.05 = Significant at 5% level

**P<0.01 = Significant at 1% level

et al., 1965). A transient and fluctuating count of monocyte, eosinophil was recorded in all the three treatment groups which varied non significantly.

Biochemical parameters

A significant ($P<0.01$) increase in serum glucose (Table 2) concentration from 60 to 120 minutes interval was seen following administration of various drug combination epidurally in animals of all the 3 groups. However, the values of glucose increased significantly ($P<0.01$) from 30 minutes interval in group A and C as compared to group B (ketamine) animals. Thereafter, the glucose level returned gradually to near normally. Hyperglycaemia might have resulted due to increased concentration of adreno-cortical hormone in blood or increased sympathetic activity and suppression of microsomal enzymes (Thurmon *et al.*, 1978) or increased glucose production in liver (Tranquilli *et al.*, 2007). These findings simulates with the observations reported by Raidurg *et al.* (1995) in cow calves.

The decrease in plasma total protein between 1 to 2 h periods following epidural injection of various drugs was non-significant in animals of all the groups. This decrease could be attributed to the increased levels of glucocorticoids, adrenal activity and increased protein turn over resulting in decreased plasma protein and albumin. It is also mentioned that decreased insulin level may modify general metabolism and impair protein synthesis and adrenal steroids also reduce the rate of protein synthesis by antagonizing the effect of insulin (Turner and Bagnara, 1976).

A significant ($P<0.01$) increase in the values of serum urea nitrogen and creatinine between 60 to 120 minutes post epidural injection was recorded in all the groups (Table 2). Serum urea nitrogen showed a significant ($P<0.05$)

increase between 1 to 2 h in all the groups during post-injection period. This might be attributed to the temporary inhibitory effect of drugs on renal blood flow, which in turn might have caused a rise in serum urea nitrogen (Kinjavdekar, 1998). A significant ($P<0.01$) increase in Aspartate aminotransferase (AST) in groups A and C at 1 h and between 1 to 2 h of observation but in group B, a non significant increase was observed. This might be due to the hypoxia produced due to respiratory centre depression in group A and C due to systemic absorption of xylazine. Alpha-2 agonists including xylazine are potent CNS depression agents. Some alternations might also take place in cell membrane permeability which may permit these enzymes to leak from the cells with intact membrane. As the values returned to pre-administration level by 24 h of observation and the values were which the normal physiological range, possibility of pathological changes in liver could therefore, be ruled out. It corroborates with the findings of Koichev *et al.* (1988) after detomidine administration in cattle and sheep. Non significant changes in group B suggested that changes in AST in groups A and C could be attributed to the effect of xylazine alone.

These observations on various haemato-biochemical parameters suggested that the alterations recorded at various time intervals following epidural injection of xylazine, ketamine along with its combination were not of great magnitude. The changes were transient and more or less same in animals of all the groups and returned to base levels within 24 h. Thus, xylazine, ketamine alone or along with its combination can be safely used for epidural anaesthesia in bovines.

SUMMARY

Haemato-biochemical response to lumbar epidural anaesthesia using xylazine, ketamine alone and its combination in buffalo calves has been reported.

REFERENCES

- Clarke, K.W. and L.W. Hall. 1969. Xylazine—a new sedative for horses and cattle. *Vet. Rec.*, **85**: 512-517.
- Jain, N.C. 1986. *Schalm's Veterinary Haematology*, 4th ed. Lea and Febinger, Philadelphia. 1221p.
- Kerr, D.C., E.W. Jones, D. Holbert and K. Huggins. 1972. Comparison of the effects of xylazine and acetylpromazine maleate in the horse. *Am. J. Vet. Res.*, **33**: 777-784.
- Kinjavdekar, P. 1998. *Spinal analgesia with alpha-2 agonists and their Combinations with ketamine and lignocaine in goats*. Ph.D. Thesis, Indian Veterinary Research Institute Deemed University, Izatnager (Uttar Pradesh), India.
- Koichev, K., D. Golemanov, H. Houbenov and B. Aminokov. 1988. Experimental study on the effect of “Domosedan” in sheep and cattle. *Journal Association of Veterinary Anaesthetist*, **15**: 114-116.
- Raidurg, R., B.N. Ranganath, S.M. Jayadevappa and C.L. Srinivas. 1995. Study of xylazine as an epidural. *Indian Vet. J.*, **72**: 894-895.
- Ryder, S., W.L. Way and A.J. Trevor. 1978. Comparative pharmacology of the optical isomers of ketamine in mice. *International Journal of Pharmacology*, **49**: 15-23.
- Sharda, R., G.K. Dutta, S.K. Tiwari and N. Sharda. 2008. Effect of xylazine, Ketamine and their combination as epidural anaesthesia in buffalo calves. *Indian Vet. J.*, **85**: 608-610.
- Smith, D.J., A.J. Azzaro, S.B. Zaldivar, S. Palmer and H.S. Lee. 1981. The properties of the optical isomers and metabolites of ketamine on the high affinity transport and catabolism of monoamines. *Neuropharmacology*, **20**: 391-396.
- Snedecor, G.W. and W.G. Cochran. 1994. *Statistical Methods*, 8th ed. East West Press, New Delhi. 254-268.
- Soliman, M.K., S.E. Amrousi and M.Y. Khamis. 1965. The influence of tranquilizers and barbiturate anaesthesia on the blood picture and electrolytes of dogs. *Vet. Rec.*, **77**: 1256.
- Thurmon, J.C., D.R. Nelson, S.M. Harsfield and C.A. Rumore. 1978. Effects of xylazine hydrochloride on urine in cattle. *Aust. Vet. J.*, **54**(4): 178-180.
- Tranquilli, W.J., J.C. Thurmon and K.A. Grim. 2007. *Lumb and Jones, Veterinary Anaesthesia and Analgesia*, 4th ed. Blackwell Publishing, USA. 45-57.
- Turner, C.D. and J.T. Bagnara. 1976. *General Endocrinology*, 6th ed. W.B. Saunders Company, Philadelphia, London.
- Wagner, A.E., W.W. Miur and K.W. Hinchoff. 1991. Cardiopulmonary effects of xylazine and detomidine in horses. *Am. J. Vet. Res.*, **52**(5): 651-657.
- White, P.F., J. Ham, W.L. Way and A.J. Trevor. 1980. Pharmacology of ketamine isomers in surgical patients. *Anesthesiology*, **52**(3): 231-239.