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Bupivacaine with and without detomidine and ketamine for epidural analgesia in buffalo calves - Clinico-physiological study

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ABSTRACT

The present study was conducted on 15 healthy non-descript, male buffalo calves aging 6 to 8 months to evaluate the efficacy of bupivacaine alone and in combination with ketamine and detomidine for lumbar epidural analgesia. The calves were randomly divided into 3 groups, viz. group A (bupivacaine alone), group B (bupivacaine and ketamine), and in group C (bupivacaine and detomidine) were administered. The onset of analgesia was significantly earlier in group C animals (5.65 ± 1.86 min) as compared to group B (5.87 ± 1.77 min) and group A (10.73 ± 2.82 min). In group A animals, analgesia was mild to moderate of thorax and flank, while it was moderate to complete in group C and B. In inguinal, perineum, hind limbs and tail regions analgesia was mild to moderate in group C, whereas it was very mild to mild in group A and B. The duration of analgesia and recovery time was significantly longer in group C than in groups A and B. The mean respiration rate and heart rate decreased significantly in groups A and C, whereas it increased significantly in group B.

Key words: Buffalo, Bupivacaine, Calves, Detomidine, Ketamine, Lumbar epidural

Bupivacaine hydrochloride is approximately four-times more potent than lignocaine hydrochloride and provides period of analgesia at least twice as that of lignocaine, and is well tolerated by all tissues (Hall 1971). Ketamine hydrochloride is a congener of phencyclidine and its positive isomer is more potent than negative isomer for analgesic properties (White *et al*. 1980). Detomidine [4(5)-(2, 3-dimethyl benzyl) imidazole hydrochloride] is a veterinary analgesic and sedative compound and induces its effect via stimulation of central α-2 adreno receptors (Virtanen *et al*. 1985). Reports regarding clinical use of bupivacaine alone and in combination with detomidine and ketamine in buffaloes are limited. Therefore, the research work was planned to elucidate the clinico-physiological effect of these combination in buffalo calves.

MATERIALS AND METHODS

Clinically healthy non-descript, male buffalo calves (15), 6 to 8 months old, weighing between 55 and 75 kg were dewormed with albendazole @ 7.5 mg/kg body weight orally one month before the start of experiment. They were kept off-fed for 24 h and water was withheld for 12 h prior to the start of the experiment. The animals were divided randomly into 3 groups of 5 animals each. In group A, only bupivacaine @ 0.15 mg/kg body wt, in group B bupivacaine @ 0.15 mg/kg body wt and ketamine @ 2.5 mg/kg body wt and in group C bupivacaine@ 0.15 mg/kg body wt and detomidine @ 15 mgm/kg body wt was administered at lumbar epidural space taking aseptic precautions.

Clinical observations, viz. onset, depth of analgesia, area of desensitization, motor inco-ordination, sedation and salivation, were recorded before (0 min) and at 5, 10, 15, 20, 30, 45, 60, 75, 90, 105 and 120 min after administration of drugs. Time from epidural injection of drug(s), to loss of sensation at thoracic/abdominal region was considered as time of onset of analgesia. Depth of analgesia and area of desensitization was recorded at thorax, flank, inguinal region, hind limbs, perineum and tail by observing response to pinpricks at a particular region and were graded on a 0 to 3 score scale, i.e. strong reaction to pin pricks (0/no analgesia), weak response to pin pricks (1, mild analgesia), occasional response to pin pricks (2, moderate analgesia), and no response to pin pricks (3, complete analgesia).

The motor inco-ordination was graded on a 0 to 4 score scale, i.e walking without staggering (0), able to stand but walks with little inco-ordination (1), able to stand but walks

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with extreme inco-ordination (2), sternal recumbency but animal is able to flex and extend the limbs if disturbed (3), and sternal recumbency and animal is unable to flex or extend its limbs (4). The heart-rate, respiration rate and rectal temperature (°F) were recorded before and at 10, 15, 30, 45, 60, 75, 90, 105, 120 and 180 min after injection of drug(s). Ruminal movements were recorded at every 30 min from paralumbar fossa after the injection of drug(s) up to complete recovery and 24 h after the injection. Onset, persistency and cessation of salivation were also recorded.

RESULTS AND DISCUSSION

The onset of analgesia was significantly (P<0.01) earlier in group C (5.65 ± 1.86 min) animals as compared to group A (10.73 ± 2.82 min) and group B (5.87 ± 1.77 min). The early onset of analgesia in group C might be due to high lipophilicity of detomidine as also reported by Pratap *et al*. (2000) after epidural administration of alpha 2 agonists in buffalo calves.

Depth of analgesia and area of desensitization at thorax and flank region in group A animals was moderate, whereas in group B and C animals it was complete between 30 and 60 min post-injection. At inguinal, hind limb and perineum region, it was mild in group A and mild to moderate in group B and C with peak effect between 45 and 75 min. In tail, depth of analgesia was very mild to mild in all the animals.

Analgesia produced by ketamine is mediated by various pathways especially opiate receptors and lamina-specific inhibition of dorsal horn activity. Further, it is established that ketamine is a potent non-competitive antagonist of NMDA receptors, which are involved in the transmission and modulation of nonreceptive information at the spinal cord level (Yamamura *et al.* 1990). The anaesthesia induced by bupivacaine with detomidine combination was deeper and prolonged. Longer duration of analgesia produced by alpha-2 agonists is attributed to the fact that alpha-2 adrenoceptor agonists provide a local depot of the drug from where they are released slowly for a longer period of time (Nolan and Erhardt 1990).

Salivation was absent in group A, whereas it was mild in group B and extreme in group C animals which might be due to decreased swallowing reflex by alpha-2 agonists in ruminants (Knight 1980). Detomidine might have also caused salivation through a similar mechanism involving CNS effects of α-2 adrenergic agonists leading to increased salivation.

Animals of group B and C showed significantly (P<0.01) longer duration of analgesia, i.e. 111.48 ± 3.85 min and 168.67 ± 4.34 min, respectively, as compared to animals of group A (93.34 ± 3.68 min). Recovery time was significantly (P<0.01) longer in group C animals (179.54 ± 3.18 min) as compared to group A (111.23 ± 3.52 min) and group B (123.31 ± 3.38).

The mean heart rate and respiration rate decreased significantly (P<0.05) between 30 and 75 min in group A and C whereas in group B, a significant (P<0.05) increase in heart rate and respiration rate was observed between 30 and 60 min. A significant (P<0.05) decrease in mean rectal

Table 1. Effect on heart rate (beats/min), respiration rate (per min) and rectal temperature (°F) in different groups at various time interval

Parameter	Group	Time interval (min)										
		0	10	15	30	45	60	75	90	105	120	180
Heart rate (beats /min)	A	49.80 ±1.15	49.65 ±1.02	49.62 ±0.92	49.15 ±1.01*	48.00 ±1.11*	47.20 ±1.46*	46.25 ±1.52*	47.00 ±1.32	47.55 ±1.39	48.10 ±1.28	48.45 ±1.36
	B	49.40 ±1.02	52.40 ±1.02	54.60 ±0.97	57.80 ±0.96*	60.40 ±0.81*	58.80 ±0.86*	57.00 ±0.89	55.8 ±0.86	55.20 ±1.01	53.80 ±1.19	51.00 ±1.18
	C	55.00 ±2.68	52.20 ±2.61	49.40 ±2.87*	42.20 ±2.51**	38.60 ±2.33**	36.32 ±2.33**	35.96 ±2.17**	35.85 ±1.51**	46.23 ±2.14**	50.45 ±2.21	53.37 ±2.22
Respiration rate(/min)	A	15.60 ±0.67	15.54 ±0.48	15.05 ±0.37	14.45 ±0.31	13.75 ±0.39*	13.48 ±0.50*	13.15 ±0.50*	13.92 ±0.70	14.00 ±0.70	15.15 ±0.50	15.32 ±0.50
	B	16.20 ±0.79	16.68 ±0.92	17.22 ±1.20	18.40 ±1.39*	20.32 ±1.44*	21.74 ±1.79*	20.18 ±1.87	18.28 ±1.77	17.72 ±1.63	17.51 ±1.49	16.75 ±0.81
	C	15.40 ±0.74	13.12 ±0.67	11.75 ±0.66*	9.68 ±0.58**	9.52 ±0.50**	8.62 ±0.50**	8.60 ±0.58**	11.13 ±0.58*	12.42 ±0.59	13.51 ±0.50	14.78 ±0.37
Rectal temp. (°F)	A	100.68 ±0.25	100.44 ±0.27	100.44 ±0.27	100.00 ±0.28	99.80 ±0.28	99.52 ±0.27	99.44 ±0.23*	99.00 ±0.15*	98.60 ±0.47	99.40 ±0.20	100.12 ±0.14
	B	99.88 ±0.35	99.84 ±0.40	99.60 ±0.38	99.16 ±0.36	98.96 ±0.36	98.88 ±0.36	99.28 ±0.36*	99.16 ±0.35*	99.28 ±0.36	99.44 ±0.35	99.76 ±0.37
	C	100.68 ±0.23	100.44 ±0.26	100.04 ±0.26	99.60 ±0.26*	99.60 ±0.26*	99.40 ±0.26*	99.38 ±0.23*	99.32 ±0.23*	99.12 ±0.23*	99.36 ±0.23*	99.88 ±0.28

* P < 0.05; ** P < 0.01

temperature was observed between 75 and 90 min in all the animals. However, the values returned to near normalcy by 180 min (Table 1).

Bradycardia in group A animals might be due to paralysis of cardiac sympathetic fibres or a generalized decrease in the sympathetic activity (Lumb and Jones 2007). Tachycardia in group B might be due to sympathomimetic action primarily and by direct stimulation of CNS by katamine. Bradycardia was more pronounced in group C, which might be attributed to decreased sympathetic outflow from the CNS, inhibition of norepinephrine (NE) release from sympathetic nerve terminals, direct depression of cardiac pacemaker and conduction tissue, increased vagal tone, and a direct increase in the release of acetylcholine from parasympathetic nerves in the heart following epidural administration of alpha 2 agonists as also reported by McDonald and Virtanen (1992).

Decrease in respiration rate might be due to depression of the respiratory centre through stimulation of supraspinal adrenoreceptors following systemic absorption of the drugs (Prado *et al*. 1999). The increase in respiration rate in group B might be due to the stimulatory action of ketamine on the respiratory centre. The decrease in rectal temperature might be due to reduced basal metabolic rate, muscle activity and depression of thermoregulatory centre (Ponder and Clarke 1980). The transient changes in the physiological parameters were compensated within 6 h.

Ruminal movements decreased significantly ($P<0.01$) between 60 and 120 min in group C animals only which might be due to binding of alpha-2 agonist drug to alpha-2 adrenergic receptors in the CNS and fore-stomach muscles, thereby inhibiting reticulo-ruminal contractions as also observed by Ruckebusch and Allal (1987) after administration of alpha-2 agonists in cattle.

Thus detomidine and ketamine in combination with bupivacaine can be safely used as lumbar epidural anaesthetics in buffaloes.

REFERENCES

Hall L W. 1971. Local analgesia. *Wright's Veterinary Anaesthesia and Analgesia*.7th edn. Bailliere Tindall, London. pp. 39.

Knight A P. 1980. Xylazine. *Journal of American the Veterinary Medical Association* **176**: 453–54.

Lumb W V and Jones E W. 2007. *Spinal Anaesthesia in Veterinary Anaesthesia*. 4th edn. Lea Febiger, Philadelphia.

MacDonald E and Virtanen R. 1992. Review of the pharmacology of medetomidine and detomidine. Two chemically similar á$_2$-adrenoceptor agonists used as veterinary sedatives. *Animal Pain.* pp. 181–91. (Eds) Short C E and Poznak A V. Churchill Livingstone, New York.

Nolan A M and Erhardt W. 1990. The cardiopulmonary effects of intrathecal xylazine in the conscious rabbit. *Journal of Veterinary Pharmacology and Therapeutics* **13**: 29–35.

Ponder S W and Clark W G. 1980. Prolonged depression of thermoregulation after xylazine administration in cats. *Journal of Veterinary Pharmacology and Therapeutics* **3**: 203–07.

Prado M E, Streeter R N, Mandsager R N, Shawley R V and Claypool P L. 1999. Pharmacologic effects of epidural versus intramuscular administration of detomidine in cattle. *American Journal of Veterinary Research* **60**: 1242–47.

Pratap K, Amarpal and Kinjavdekar P. 2000. Comparison of xylazine and bupivacaine for lumbosacral epidural analgesia in buffalo calves. Abstract 24th Congress of ISVS held at Mannuthy, Kerala. Nov. 10–12.

Ruckebusch Y and Allal C. 1987. Depression of reticulo-ruminal motor functions through the stimulation of alpha-2 adrenoceptors. *Journal of Veterinary Pharmacology and Therapeutics* **10**: 1–10.

Virtanen R, Ruskoaho H and Nyman L. 1985. Pharmacological evidence for the involvement of á2-adrenoceptors in the sedative effect of detomidine, a novel sedative analgesic. *Journal of Veterinary Pharmacology and Therapeutics* **8**: 30.

White P P, Ham J, Way W L and Trevor A J. 1980. Pharmacology of ketamine isomers in surgical patients. *Anesthesiol*ogy **52**: 231.

Yamamura T, Harada K, Okamura A and Kemmotsu O. 1990. Is the site of action of ketamine anaesthesia the N-methyl-D-aspartate receptor? *Anaesthesiology* **72**: 704–71