Comparative evaluation of ropivacaine, bupivacaine and xylazine -ketamine combination for epidural analgesia in goats

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SINGH, K., P. KINJAVDEKAR, A. GOPINATHAN, H. P. AITHAL, M. VERMA, AMARPAL: Comparative evaluation of ropivacaine, bupivacaine and xylazine-ketamine combination for epidural analgesia in goats. Vet. arhiv 85, 151-162, 2015. ABSTRACT

The study was conducted on eighteen healthy non-descript male goats divided into 3 groups: A, B and C, having 6 animals in each. Lumbosacral epidural ropivacaine (0.6 mg/kg), bupivacaine (0.5 mg/kg) and xylazine and ketamine (0.025 mg/kg and 2.5 mg/kg) were administered in groups A, B and C, respectively. The treatments were compared using clinical, physiological, haematological, biochemical and acid base/blood gas parameters. The earliest onset of analgesia was produced by epidural xylazine and ketamine combination. Xylazine and ketamine, bupivacaine and ropivacaine produced complete analgesia of the tail, perineum, inguinal region and thighs for variable intervals. The xylazine and ketamine combination produced analgesia of a greater extent and longer duration, followed by bupivacaine and ropivacaine. Mild sedation was produced by the xylazine and ketamine combination alone. Recovery was faster with ropivacaine, followed by bupivacaine and the xylazine and ketamine combination. The xylazine and ketamine combination produced a non-significant decrease in the heart rate and respiratory rate of the animals. There were insignificant fluctuations in pCO₂, pO₂, SO₂, pH and HCO₃ values from base line at different intervals in all the groups. The changes in haematobiochemical and blood electrolyte values were transient, and hence of little significance in all the groups. The results of this study suggest that all these drugs could be considered safe for epidural analgesia in the administered doses for healthy goats.

Key words: bupivacaine, epidural analgesia, goats, ketamine, ropivacaine, xylazine

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Introduction

Bupivacaine has been used spinally for pre-emptive and posttraumatic analgesia in buffalo calves (PATHAK et al., 2012) and for epidural anaesthesia in normal and uraemic goats (SINGH et al., 2007a). Xylazine has been used to induce sacrococcygeal/lumbosacral spinal analgesia in different species of animals and produces a longer duration of regional analgesia (KINJAVDEKAR et al., 2007; SINGH et al., 2007b). The xylazine and ketamine combination has been used for epidural/spinal anaesthesia in healthy goats (KINJAVDEKAR et al., 2007; SINGH et al., 2007b) and buffalo calves (SINGH, 2001) with minimal systemic effects. The potency of ropivacaine is reported to be similar to that of bupivacaine but four times more than that of mepivacaine (AMARPAL et al., 2007). It has been used for epidural analgesia in buffalo calves (AMARPAL et al., 2007) and goats (SINGH et al., 2005). GANIDAGLI et al. (2004) also induced satisfactory caudal epidural analgesia in mares with 0.5 per cent ropivacaine, though a transient fall in systolic blood pressure was recorded. Epidural/spinal anaesthesia has been shown to have less cardiopulmonary and other systemic side effects than general anaesthesia in ruminants (HALL et al., 2001). The advantages of lumbosacral epidural analgesia over general anaesthesia in goats have been described by SINGH et al. (2007a). Lumbosacral epidural analgesia may be used for surgery involving the hind limbs, caudal abdomen and pelvic region of goats.

The present study was designed to assess and compare the effects of ropivacaine, bupivacaine, and a xylazine-ketamine combination on the clinical, physiological and haematobiochemical parameters in goats.

Materials and methods

The present study was carried out to compare the lumbosacral epidural analgesia produced by ropivacaine (0.6 mg/kg) (group A), bupivacaine (0.6 mg/kg) (group B) and a combination of ketamine (2.5 mg/kg)-xylazine (0.025 mg/kg) (group C) in 18 clinically healthy, non-descript male goats of 6 to 9 months of age. All the animals were maintained under uniform feeding and management conditions and were acclimatized to approaching and handling during this period. The doses of different anaesthetics were selected after conducting pilot trials in a few goats before the start of the study. The animals were restrained in a standing position and the lumbosacral region was prepared for epidural injection. A 20-gauge, 4 cm long hypodermic needle was inserted along the midline. The needle was advanced at an angle of 70° to the skin surface cranioventrally, up to a depth of 2-3 cm depth. The correct position of the needle was ascertained by loss of resistance to the injection. Under surgical analgesia post-scrotal urethrotomy was performed uniformly. The surgical procedure and the extent of trauma were similar in all the animals. The treatments were evaluated and compared on the basis of clinical, physiological, and haematobiochemical parameters.

The base line values (0) for all the parameters were taken before the injection of the drug (s). Response to pin picks was recorded at the perineal region every 5 sec until sensation was lost. The time from injection to loss of sensation was considered as the time of onset of analgesia (sec). The depth and extent of analgesia was recorded by making pin pricks at the perineum, the inguinal region, the upper part of the hind limbs, the digits, flank, thorax and ventral abdomen at 0, 5, 10, 15, 20, 30, 45, 60, 75, 90, 105 and 120 minutes after injection of drugs. Depth of analgesia was graded on a 0-3 scale where 0 = no analgesia, strong reaction to pinpricks; 1 = mild analgesia, weak response to pinpricks; 2 = moderate analgesia, occasional response to pinpricks; 3 = complete analgesia, no response to pinpricks (SINGH et al., 2007b). Sedation was also evaluated at the same time intervals and was graded on a 0-4 scale as: 0 = standing alert; 1 = standing but tired with slight lowering of the head and ptosis of eyelids; 2 = standing with wide stance and extreme lowering of head; 3 = animal attained recumbency but could sit without support; and 4 = lateral recumbency (SINGH et al., 2007b).

Time (min) from loss of sensation to a return of sensation in the perineal region was considered as the duration of analgesia. All the animals were observed up to their standing recovery (min) when they started walking without support. During the period of analgesia the animals were also observed for the extent of salivation and frequency of urination. Heart rate (beats/min) (HR), respiratory rate (breaths/min) (RR) and rectal temperature (°C) (RT) were recorded at the same time intervals (min) as for analgesia. Animals were also observed for their response to skin incision and to any other stimuli during surgery. Additional doses of drug required or use of local anaesthetic as infiltration analgesia, if needed, were also recorded.

A total of 5 mL of venous blood was collected in 2 separate vials (4 mL in heparin and 1 mL in sodium fluoride) before and at 30, 60 and 120 min after injection of drugs. Freshly heparinized blood was utilized for estimation of the haemoglobin (Hb, g/L), hematocrit (%), total leukocyte count (TLC, $\times 10^9$ /L) and differential leukocyte count (DLC, %).

Plasma was used for estimation of urea nitrogen (mmol/L), creatinine (μmol/L) and total protein (mmol/L). Plasma collected in sodium fluoride was used for estimation of glucose (mmol/). The fresh heparinized venous blood was utilized for estimation of pH, pO₂ (mmHg), pCO₂ (mmHg), SO₂ (%), base excess (mmol/L), HCO₃ (mmol/L).

Statistical analysis. Analysis of variance (ANOVA) and Duncan's Multiple Range Test (DMRT) were used to compare the means between different groups at corresponding intervals. The paired "t" test was used to compare the mean values at different intervals with the base values in each group. The subjective parameters were analysed using the Wilcoxon signed rank test.

Results

The time of onset of analgesia in animals in groups A, group B and group C was $22-40 \pm 7$ sec, $17-41 \pm 9$ sec and $23-31 \pm 5$ sec, respectively. The time of onset of analgesia did not differ significantly (P<0.05) among these groups.

In groups B and C significantly (P<0.05) higher analgesia of the tail was recorded at 30, 45, 60, 75, 90, 105 and 120 min intervals as compared to group A. The tail analgesia of group C was significantly (P<0.05) higher at the 105 min interval than B. Perineal analgesia of groups B and C was significantly (P<0.05) higher than A after 30 min of observation. Inguinal analgesia in groups B and C was significantly (P<0.05) higher than that in group A at 30 min and onwards. A significantly (P<0.05) greater depth of analgesia of the digits was recorded in group C than in groups A and B. At 5, 90, 105 and 120 min intervals analgesia was significantly (P<0.05) greater in group C than in group B. Comparison of the groups showed that C had significantly (P<0.05) higher and longer duration of analgesia on the caudal flank than groups B and A at all intervals. Group B showed significantly (P<0.05) greater analgesia at all intervals than A. Comparison of the groups showed that group C had significantly (P<0.05) greater depth and longer duration of analgesia in that cranial flank than groups A and B at all intervals.

The duration of analgesia in animal groups A, B and C was recorded as 71.5 ± 14.4 min, 120.75 ± 8.8 min and 127.25 ± 6.8 min, respectively. Duration of analgesia was significantly (P<0.05) shorter in group A, as compared to B and C. But no significant (P>0.05) difference was observed between groups B and C.

Only in group C was mild sedation noticed at 5 and 10 min then moderate sedation up to 60 min and it gradually vanished thereafter.

The mean values for recovery time in groups A, B and C were 83.25 ± 16.9 min, 128.57 ± 5.8 min and 136 ± 7.3 min respectively. Recovery time was significantly (P<0.05) shorter in group A as compared to B and C. However, between groups B and C the difference in recovery time was non-significant (P<0.05).

Mild salivation was noticed only in group C from the 15 min interval up to the end of observation. Animals of different groups did not show any specific pattern of urination after drug(s) administration. No response to surgical stimuli in the perineal region was observed in any group. The depth of analgesia in the perineal region was sufficient to perform surgery at this site. No additional dose of drug(s) was required while the surgery was in progress nor infiltration with local anaesthetic solution at the site.

In group A, HR decreased and remained below the base line up to 120 min. In group B after a non-significant (P>0.05) increase up to 15 min, HR decreased non-significantly (P>0.05) below the base line thereafter. A significantly (P<0.05) lower respiratory rate from the base value was observed in group C at the 15 min interval (P<0.05) and at the

90 min interval (P<0.05). Among groups A, B and C there were no significant differences in RR. Among the groups, significantly (P<0.05) lower RT was noticed in C than in A and B from 60 min onwards. In groups A and B it did not differ significantly (P>0.05) at various intervals (Fig. 1).

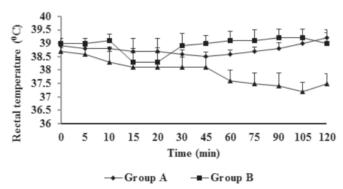


Fig. 1. Rectal temperature (°C) recorded in animals of different groups

Table 1. Mean \pm SE values of haematological parameters in animals of different groups

		Interval (min)				
Parameters	Groups	0	30	60	120	
Hb (g/L)	A	87.5 ± 2.50	84.20 ± 1.43	84.50 ± 2.03	$80.75 \pm 2.40^*$	
	В	85.25 ± 4.08	83.25 ± 3.93	83.50 ± 3.66	80.75 ± 5.33	
	С	85.00 ± 7.07	78.00 ± 3.66	80.00 ± 4.66	81.50 ± 4.66	
Hematocrit (%)	A	26.2 ± 0.89	25.12 ± 0.43	25.42 ± 0.61	24.30 ± 0.72	
	В	26.95 ± 1.0	26.17 ± 1.18	26.5 ± 1.1	25.7 ± 1.6	
	С	25.2 ± 1.9	23.8 ± 1.1	24.5 ± 1.4	24.6 ± 1.4	
TLC (×10 ⁹ /L)	A	10.86 ± 0.31^{b}	10.5 ± 0.31^{b}	10.4 ± 0.30	10.5 ± 0.28^{b}	
	В	12.8 ± 1.0^{b}	12.8 ± 1.0^{b}	12.6 ± 1.0^{b}	12.5. ± 1.0 ^b	
	С	10.9 ± 0.49^{b}	10.9 ± 0.79^{b}	10.9 ± 0.85^{b}	10.9 ± 0.84^{b}	
Neutrophils (%)	A	39.5 ± 0.28^{b}	39.2 ± 0.25^{a}	39 ± 0.40	39.5 ± 0.64	
	В	37 ± 1.0^{b}	37.25 ± 1.1^{a}	36.75 ± 1.4	37.7 ± 1.1 .	
	С	35.7 ± 0.94^{a}	36.5 ± 0.95^{b}	37 ± 1.0	38.25 ± 1.1	
Lymphocytes (%)	A	56.7 ± 0.47	57 ± 0.40	57.5 ± 0.86	56.7 ± 0.47^{a}	
	В	56.75 ± 1.3	56.75 ± 1.3	56.25 ± 1.7	56.00 ± 1.2^{a}	
	С	57.2 ± 1.1	56.5 ± 1.04	56.2 ± 1.1	$54.75 \pm 0.94^{ab**}$	

Values with different alphabets differ significantly (P<0.05) at corresponding intervals; * Differ significantly (P<0.05) from preinduction values; ** Differ significantly (P<0.01) from preinduction values

Table 2. Mean \pm SE values of different biochemical in animals of different groups

		Interval (min)				
Parameters	Groups	0	30	60	120	
Urea Nitrogen (mmol/L)	A	5.0 ± 0.67	4.9 ± 0.59	5.2 ± 0.68	4.5 ± 1.5	
	В	$4.4 \pm .11$	4.7 ± 1.2	5.1 ± 1.2	5.4 ± 1.2	
	C	3.4 ± 0.61	3.9 ± 0.68	3.8 ± 0.52	3.8 ± 0.55	
Creatinine	A	102.2 ± 13.13	106 ± 11.5	119 ± 8.3	111 ± 8.1	
	В	106.5 ± 2.9	106.5 ± 6.8	106.5 ± 4.3	111.25 ± 4.1	
(μmol/L)	C	92 ± 14.7	96.2 ± 12.5	105.5 ± 14.5	106.25 ± 14.9	
Glucose	A	27.6 ± 0.21	27.5 ± 0.26	28.0 ± 0.19	27.7 ± 0.28	
	В	27.3 ± 0.18	27.1 ± 0.25	26.9 ± 0.16	26.9 ± 0.22	
(mmol/L)	C	23.2 ± 0.09	31.1 ± 0.70	$29. \pm 0.11$	28.03 ± 0.17	
Total protein	A	7.09 ± 0.74	6.03 ± 0.24	7.02 ± 0.92	7.25 ± 0.72	
	В	5.7 ± 0.35	5.8 ± 0.36	6.7 ± 0.73	6.2 ± 0.66	
(mmol/L)	C	7.5 ± 1.00	7.32 ± 1.2	5.5 ± 1.2	6.4 ± 0.74	

Haemoglobin remained within the normal range throughout the period of observation in all the groups (Table 1). In groups A, B and C lower haematocrits were noticed at 30, 60 and 120 min. In all the groups a gradual increase in TLC at 30, 60 and 120 min was recorded (Table 1). In groups A, B and C there was slight and non-significant variation in neutrophils at different time intervals. Group A showed significantly (P<0.05) higher neutrophils at 0 and 30 min in comparison to group C. Significantly (P<0.05) lower monocytes were recorded at 30, 60 and 120 min interval in group A than groups B and C. Group B recorded significantly (P<0.05) higher eosinophils at 0 and 120 min intervals than groups A and C (Table 1).

Urea nitrogen, creatinine, total protein, glucose (Table 2), pCO2 pO2, HCO3, PH and oxygen saturation (SO2) (Table 3) did not differ significantly (P>0.05) between the groups at different intervals. In all groups the base excess (BE) value increased non-significantly, except in group C where a significant (P>0.05) increase at 60 and 120 min was noticed.

Table 3. Mean \pm SE values of different blood gas parameters in animals of different groups

		Interval (min)				
Parameters	Groups	0	30	60	120	
pCO ₂ (mmHg)	A	49.2 ± 2.9	47.1 ± 3.5^{b}	46.0 ± 3.3 ^{b*}	$43.6 \pm 3.4^{ab**}$	
	В	47.1 ± 1.6	45.8 ± 1.2^{b}	45.3 ± 2.8^{b}	43.3 ± 1.4^{ab}	
	С	53.7 ± 3.2	56.3 ± 3.9^{a}	54.7 ± 4.4^{a}	50.17 ± 4.7^{a}	
pO ₂ (mmHg)	A	26.9 ± 0.92	28.5 ± 3.0	28.5 ± 1.0^{ab}	27.3 ± 1.5	
	В	26.9 ± 1.4	28.0 ± 1.9	26.2 ± 2.4^{b}	30.3 ± 2.3	
	C	33.77 ± 4.6	32.4 ± 6.4	29.6 ± 3.3^{ab}	31.4 ± 3.8	
SO ₂ (%)	A	43.45 ± 3.5	48.1 ± 8.0	50.2 ± 3.0^{ab}	48.2 ± 5.0	
	В	43.8 ± 5.2	46.7 ± 2.2	42.2 ± 5.0^{b}	54.12 ± 3.2	
	C	50.15 ± 9.2	47.37 ± 12.2	48 ± 8.7^{ab}	$53.4 \pm 10.$	
рН	A	7.34 ± 0.030^{a}	7.36 ± 0.030	7.38 ± 0.026	7.4 ± 0.019	
	В	$7.34 \pm 0.034^{\rm a}$	7.36 ± 0.05	7.37 ± 0.05	7.39 ± 0.03	
	C	7.24 ± 0.01^{b}	7.23 ± 0.24	7.32 ± 1.0	7.35 ± 0.73	
Bicarbonate (mmol/L)	A	5.0 ± 1	$5.25 \pm .62$	6.25 ± 1.37	5.25 ± 1.10	
	В	7.5 ± 1	6.7 ± 0.62	7.2 ± 1.3	7 ± 1.1	
	C	4.75 ± 1.18	5.75 ± 1.03	6.25 ± 0.62	6.75 ± 0.85	
BE (mmol/L)	A	-1.27 ± 2.22^{b}	-1.50 ± 2.65 ^b	-1.325 ± 1.91	-1.95 ± 1.13	
	В	-2.35 ± 2.12^{b}	-2.32 ± 2.11^{b}	-2.31 ± 2.29	-2.31 ± 2.44	
	С	-1.35 ± 0.80^{a}	-1.34 ± 0.94^{a}	$1.12 \pm 1.29^*$	$1.19 \pm 1.54^*$	

Values with different alphabets differ significantly (P<0.05) at corresponding intervals; * Differ significantly (P<0.05) from preinduction values; ** Differ significantly (P<0.01) from preinduction values

Discussion

In our study onset of analgesia did not differ significantly (P<0.05) between the groups. The fastest onset of analgesia was produced by ropivacaine followed by the combination of xylazine and ketamine, and the slowest onset was recorded with bupivacaine. AMARPAL et al. (2007) also recorded faster onset of analgesia with epidural ropivacaine in buffalo calves. Similar trends for onset of analgesia with ropivacaine (SINGH et al., 2005), bupivacaine (SINGH et al., 2007a) and the xylazine-ketamine combination were reported in goats (KINJAVDEKAR et al., 2007; SINGH et al., 2007b).

Ropivacaine, bupivacaine and the combination of xylazine and ketamine produced complete analgesia of the tail, perineum, inguinal region, and mild to moderate analgesia of the flank and digits. The local anaesthetic drugs, if applied locally to nervous tissue or injected spinally in effective concentrations, block conduction of impulses from receptors to the cerebral cortex of the brain (BOOTH, 1988). SINGH (2001) recorded mild to moderate

analgesia of the tail, perineum, inguinal region, thigh and digits with epidural bupivacaine (0.125 to 0.128 mg/kg) in buffalo calves. The lower depth of analgesia in these regions might be due to the lower doses of bupivacaine used by them in their study as compared to those used in the present study. AMARPAL et al. (2007) observed complete and prolonged analgesia of the tail, perineum, inguinal region, thigh, digits, anterior and posterior flank with 0.75 % ropivacaine in buffalo calves. Epidural ropivacaine in the present study was able to produce complete analgesia of these regions but for a shorter duration in group A, probably due to the lower concentration of the drug used in the present study as compared to the study by AMARPAL et al. (2007). Further, species variations may also affect the extent and depth of analgesia.

It was interesting to note that the combination of xylazine and ketamine produced deeper and prolonged analgesia as compared to bupivacaine and ropivacaine. Similarly KINJAVDEKAR et al. (2007) and SINGH et al. (2007b) also reported that the combination of xylazine and ketamine produced more depth and longer duration of analgesia as compared to animals injected with bupivacaine epidurally in goats. The deeper analgesia produced by the combination of xylazine and ketamine has been attributed to the synergistic interaction between epidural / spinal xylazine and ketamine as reported in goats (KINJAVDEKAR et al., 1999). The synergistic interaction between xylazine and ketamine might be due to their ability to produce spinal analgesia through different mechanisms by acting at different sites of action (HALL et al., 2001).

Sedation was noticed only in the combination group. Sedation in group C might be due to xylazine, which is an α_2 - adrenoceptor agonist and sedative. Sedation has been reported after epidural xylazine in goats (KINJAVDEKAR et al., 2007; SINGH et al., 2007b). Sedation in these animals might be attributed to the supraspinal effect of xylazine, following its systemic absorption from the epidural space, as suggested by KINJAVDEKAR et al. (1999).

The duration of analgesia was significantly shorter in the ropivacaine group as compared to the bupivacaine and xylazine and ketamine groups. AMARPAL et al. (2007) observed 6 to 7 hours duration of analgesia with 0.75 % ropivacaine (5 mL and 10 mL) given epidurally in buffalo calves. The shorter duration of analgesia with ropivacaine in the present study could be attributed to the lower concentration of ropivacaine (0.2 %) used. In the present study the xylazine and ketamine combination produced a longer duration of analgesia due to their synergistic action (KINJAVDEKAR et al., 2007; SINGH et al., 2007b). Bupivacaine produced a non-significantly shorter duration of analgesia when compared to xylazine and ketamine. A duration of analgesia similar to the present study with epidural bupivacaine was reported in goats (SINGH et al., 2007a).

A significantly longer recovery time was observed in group C than in groups B and A. Ropivacaine is a longer acting local anesthetic, which is effective when given epidurally over a wide range of concentrations (HALL et al., 2001). AMARPAL et al. (2007) observed

recovery from analgesia in 6-7 hours and 8-9 hours after epidural administration of ropivacaine (0.75 %) in 5 mL and 10 mL volume in buffalo calves. The present study showed a significantly faster recovery with epidural ropivacaine in normal goats, which could be attributed to the lower concentration of ropivacaine used (0.2 %) in this study and the species difference that might have played a role in early recovery. A similar observation after epidural administration of ropivacaine was recorded by SINGH et al. (2005). Bupivacaine, when given epidurally, exhibited slower recovery than ropivacaine. A prolonged recovery from xylazine and ketamine was observed in normal goats, which might be due to the fact that α_2 - agonists, after their absorption from the epidural space, are slowly released from the local depot in the nervous tissue (HALL et al., 2001). Similar observations were recorded in goats after epidural administration of bupivacaine (SINGH et al., 2007a) and the xylazine and ketamine combination (KINJAVDEKAR et al., 2007; SINGH et al., 2007b).

In all the groups there was a gradual decrease in HR after epidural administration of the drugs. A reduction in HR after epidural/spinal administration of bupivacaine (SINGH et al., 2007a) and ropivacaine (SINGH et al., 2005) has been reported in goats. The decrease in HR in groups C might be attributed to the action of xylazine on CNS after its systemic absorption from the venous sinuses in the epidural space. A significant decrease in HR has been considered to be a classical response following administration of α, agonists in all the species tested so far (KINJAVDEKAR et al., 1999). AITHAL et al. (1996) recorded a significant reduction in HR after epidural administration of xylazine and ketamine in normal goats. This might be attributed to the cardiac depressant action of xylazine. No significant difference in RR was noticed at different time intervals in all the groups. AMARPAL et al. (2007) in calves and SINGH et al. (2005) in goats could not find a significant change in RR after epidural administration of ropivacaine. The lack of change in RR in group C administrated with xylazine and ketamine could be attributed to the stimulatory effect of ketamine. AITHAL et al. (1996), KINJAVDEKAR et al. (2007) and SINGH et al. (2007b) reported that epidural/ subarachnoid administration of ketamine was always associated with an increase in RR in goats. A slight decrease in RT was recorded in all the groups, and it returned to base line later on, but in group C the fall in RT became significant towards the end. The significant decrease in RT in group C might be attributed to the xylazine. PONDER and CLARKE (1980) reported that α_2 - agonists produced a decrease in RT by depressing thermoregulatory centres. Similar observations of hypothermia have been observed following the use of xylazine in goats (KINJAVDEKAR et al., 2007; SINGH et al., 2007b).

Haemoglobin, haematocrit and TLC decreased gradually in all the groups up to 120 min after injection of different drugs. Pooling of the circulating blood cells in the spleen or other reservoirs secondary to decreased sympathetic activity may explain the

decrease in the Hb, hematocrit and TLC recorded in this study, as also reported with other tranquilizers in dogs. Similar findings were recorded after epidural administration of xylazine (AITHAL et al., 1996) and the xylazine and ketamine combination in goats (KINJAVDEKAR et al., 2007; SINGH et al., 2007b). The decrease in haemoglobin, hematocrit and TLC during the period of anaesthesia or sedation may also be due to shifting of fluid from the extravascular compartments to the intravascular compartment, in order to maintain normal cardiac output (WAGNER et al., 1991). The DLC showed a rise in neutrophil count and a decrease in lymphocyte count in all the groups in the present study. Similar findings were reported for epidural xylazine and ketamine (KINJAVDEKAR et al., 2007; SINGH et al., 2007b) and bupivacaine (SINGH et al., 2007a) in goats.

Creatinine, after 2 hours of drug administration, did not differ significantly between the groups. A slight increase in creatinine has been reported when xylazine and ketamine (KINJAVDEKAR et al., 2007; SINGH et al., 2007b) and bupivacaine (SINGH et al., 2007a) were used in goats. In all groups a gradual but insignificant increase in urea nitrogen was observed up to the 120 min interval. A slight increase in creatinine has been reported when medetomidine/xylazine and ketamine (KINJAVDEKAR et al., 2007 and SINGH et al., 2007b) and bupivacaine (SINGH et al., 2007a) were administered epidurally to goats. The increase in urea nitrogen was only slight and started to return to base value at 120 min and thus could not be ascribed to renal damage. A slight increase in urea nitrogen has been reported earlier, after administration of the xylazine and ketamine combination in goats (KINJAVDEKAR et al., 2007; SINGH et al., 2007b) and in buffalo calves (SINGH et al., 2005). A non-significant increase in glucose was noticed in all the groups, which was more apparent in group C. Alpha,- agonists have been reported to cause hyperglycaemia by stimulation of post synaptic α_2 - receptors in pancreatic β cells, which inhibit insulin release (HSU and HUMMEL, 1981). However, the effects of various anaesthetic drugs and their combinations on glucose seemed to be only transient because glucose levels in all the groups remained near the base value of the respective group. Total protein concentrations fluctuated near the base line throughout the period of observation and remained near to normal physiological values in all groups. The further decrease in total protein and albumin at 30 to 60 min intervals recorded in group C could be attributed to the inter-compartment shift of fluid (KINJAVDEKAR et al., 1999). A shift of fluid from extra vascular compartment to intravascular space might have also contributed to the decrease in total protein and albumin (WAGNER et al., 1991).

In general, epidural use of ropivacaine, bupivacaine and xylazine and ketamine in healthy goats did not cause any significant changes in pH, HCO₃, BE, pCO₂, pO₂ and SO₂ values. Similar findings were also reported by SINGH et al. (2005) and (SINGH et al., 2007a) in healthy and uremic goats. Moreover, the changes, if any, in acid base and blood gas parameters were only transient in nature and became normal as the effect of the drugs wore off, and thus were considered of little significance.

Conclusions

It is concluded that bupivacaine and a xylazine - ketamine combination have almost similar analgesic potency for long durations on epidural administration in goats. Ropivacaine produced a shorter duration of analgesia and may be used for short surgical procedures. All the drugs produced only transient alterations in haematobiochemical parameters and could be considered safe in the administered doses for use in goats.

References

- AITHAL, H. P., AMARPAL, K. PRATAP, G. R. SINGH (1996): Clinical effects of epidurally administered ketamine and xylazine in goats. Small Rumin. Res. 24, 55-64.
- AMARPAL, P. KINJAVDEKAR, H. P. AITHAL, G. R. SINGH, A. M. PAWDE, T. SINGH, A. SHARMA, K. PRATAP (2007): Comparison of two doses of ropivacaine for lumbosacral epidural analgesia in buffalo calves (*Bubalus bubalis*). Vet. Rec. 160, 766-769.
- BOOTH, N. H. (1988): Intrathecal and epidural anaesthesia In: Veterinary Pharmacology and Therapeutics, 6th edn. Iowa State University Press, Ames, Lowman, pp 424.
- GANIDAGLI, S., H. CETIN, H. S. BIRICIK, I. CIMATAY (2004): Comparison of ropivacaine with a combination of ropivacaine and fentanyl for caudal epidural anaesthesia of mares. Vet. Rec. 154, 329-332.
- HALL, L. W., K. W. CLARKE, C. M. TRIM (2001): General principles of local analgesia. In: Veterinary Anaesthesia, 10th ed. W. B. Saunders and Co., London, pp. 225-244.
- HSU, W. H., S. K. HUMMEL (1981): Xylazine induced hyperglycaemia in cattle: A possible involvement of alpha-2 adrenergic receptors regulating insulin release. Endocrinol. 109, 825-829.
- KINJAVDEKAR, P., G. R. SINGH, AMARPAL, H. P. AITHAL (1999): Clinical use of spinal xylazine and ketamine in ruminants. Indian Vet. J. 76, 1101-1103.
- KINJAVDEKAR, P., G. R. SINGH, AMARPAL, H. P. AITHAL, A. M. PAWDE (2007): Clinicophysiological effects of spinally administered ketamine and its combination with xylazine and medetomidine in healthy goats. Vet. Res. Commun. 31, 847-861.
- PATHAK, R., K. PRATAP, AMARPAL, P. KINJAVDEKAR, H. P. AITHAL, A. M. PAWDE, PANKAJ (2012): Comparison of bupivacaine, xylazine and buprenorphine for spinal analgesia in buffalo calves. Indian J. Vet. Surg. 33, 82-86.
- PONDER, S. W., W. G. CLARKE (1980): Prolonged depression of thermoregulation after xylazine administration to cats. J.Vet. Pharmacol.Ther. 3, 203-207.
- SINGH, K., P. KINJAVDEKAR, AMARPAL, H. P. AITHAL, A. GOPINATHAN, G. R. SINGH, T. SINGH, A. M. PAWDE, K. PRATHAP (2005): Clinicopathological and hematobiochemical effects of epidural ropivacaine in ureamic and healthy caprines. Ind. J. Vet. Surg. 26, 11-15.
- SINGH, K., P. KINJAVDEKAR, AMARPAL, H. P. AITHAL, A. GOPINATHAN, G. R. SINGH, A. M. PAWDE, K. PRATHAP (2007a): Comparison of analgesic, clinicophysiological and hematobiochemical effect of epidural bupivacaine in healthy and uraemic goats. Small Ruminant Res. 71, 13-20.
- SINGH, K., P. KINJAVDEKAR, AMARPAL, H. P. AITHAL, A. GOPINATHAN, G. R. SINGH,

- A. M. PAWDE, K. PRATHAP (2007b): Analgesic effect of epidural ketamine and Xylazine combination in the clinicophysiological and haematobiochemical parameters of uraemic and healthy goats. Vet. Res. Commun. 31, 133-142.
- SINGH, V. (2001): Alpha-2 agonists, ketamine and bupivacaine for saccrococcygeal analgesia in buffalo calves. M.V.Sc. Thesis submitted to Deemed University, IVRI, Izatnagar, Bareilly, U.P., India.
- SINGH, V., AMARPAL, P. KINJAVDEKAR, H. P. AITHAL, K. PRATAP (2005): Haematological changes following epidural administration of xylazine and Ketamine in buffalo calves. Ind. J. of Anim. Sci. 75, 178-181.
- WAGNER, A. E., W. E. MUIR, K. W. HINCHCLIFF (1991): Cardiovascular effects of xylazine and detomidine in horses. Am. J. Vet. Res. 52, 651-657.

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SINGH, K., P. KINJAVDEKAR, A. GOPINATHAN, H. P. AITHAL, M. VERMA, AMARPAL: Usporedna analiza učinkovitosti kombinacije ropivakaina, bupivakaina i ksilazin-ketamina za epiduralnu analgeziju u koza. Vet. arhiv 85, 151-162, 2015.

SAŽETAK

Istraživanje je provedeno na 18 zdravih jaraca podijeljenih u tri skupine (A, B i C). U svakoj skupini bilo je po 6 jaraca. U svrhu lumbosakralne epiduralne analgezije, skupini A bio je primijenjen ropivakain (0,6 mg/kg), skupini B bupivakain (0,5 mg/kg), a skupini C ksilazin i ketamin (0,025 mg/kg i 2,5 mg/kg). Učinci su bili uspoređeni na osnovi kliničkih, fizioloških, hematoloških, biokemijskih i acidobaznih pokazatelja te statusa plinova u krvi. Najbrži početak analgezije postignut je epiduralnom primjenom kombinacije ksilazina i ketamina. Ksilazin i ketamin, bupivakain te ropivakain izazvali su potpunu analgeziju repa, perineuma, ingvinalnog i bedrenog područja u različitim vremenskim razmacima. Najjača i najduža analgezija postignuta je kombinacijom ksilazina i ketamina. Zatim je po jačini i dužini slijedila analgezija bupivakainom pa ropivakainom. Srednje jaka sedacija postignuta je zasebnom primjenom ksilazina i ketamina. Oporavak nakon analgezije bio je najbrži pri uporabi ropivakaina, zatim bupivakaina te na posljetku kombinacije ksilazin-ketamina. Kombinacija ksilazina i ketamina izazvala je nesignifikantan pad frekvencije bila i disanja. Kod svih skupina jaraca, u različitim vremeskim razmacima, opažena su i nesignifikantna odstupanja od početnih vrijednosti za pCO₂, pO₂, SO₂, pH i HCO⁻3. Promjene hematoloških i biokemijskih pokazatelja kao i elektrolita u krvi bile su kratkotrajne i od malog značenja u svim promatranim skupinama. Rezultati pokazuju da se svi istraženi analgetici, u upotrijebljenim dozama, mogu smatrati sigurnima za epiduralnu analgeziju zdravih koza.

Ključne riječi: bupivakain, epiduralna analgezija, koze, ketamin, ropivakain, ksilazin