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Original Research Article

Clinical evaluation of epidural bupivacaine, butorphanol, and butorphanol - bupivacaine combination in goat

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ABSTRACT

Butorphanol is a synthetic opioid commonly used for epidural anesthesia in human either alone or in combination with bupivacaine but not in goat. The objective of the present study was to evaluate the analgesic effect of epidural butorphanol either alone or in combination with bupivacaine. Fifteen adult apparently healthy goats were randomized into three equal groups to receive a lumbosacral epidural injection of bupivacaine 0.5 % (0.5 mg/kg), butorphanol 1% (0.08 mg/kg) or their combination (bupivacaine 0.25 mg/kg and butorphanol 0.04 mg/kg). Animals were observed for incoordination of hind limbs, perineal pin prick and sedation at 10 minutes interval. Heart rate, respiratory rate and rectal temperature were assessed every 15 minutes. Epidural butorphanol resulted into significantly ($P < 0.05$) rapid analgesia (9.8 ± 1.1 Min) than the butorphanol– bupivacaine combination (12.8 ± 0.84 Min) and bupivacaine (16.6 ± 0.55). Butorphanol-bupivacaine combination provoked significant (($P < 0.05$) prolonged intense analgesia (208 ± 8.36 Min) compared to either bupivacaine (112 ± 8.37) or butorphanol (166 ± 5.48 Min). Ataxia accompanied administration of bupivacaine either alone or in combination with butorphanol, while sedation was observed in animals received butorphanol alone or combined with bupivacaine. No significant changes were observed in heart rate, respiratory rate or rectal temperature. The epidural administration of butorphanol-bupivacaine combination promoted longer-lasting analgesia in goats without motor disturbances compared to bupivacaine alone. This combination might prove useful clinically to provide analgesia in goats for long-duration perineal obstetrical or surgical procedures.

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1. Introduction

Pain management strategies in veterinary medicine are continued to improve together with the growing societal concern about the moral and ethical treatment of animals (Rollin, 2004). Besides improving animal welfare standards, anesthesia and analgesia are essential for easier procedures and improved safety of both animal and personnel (Anderson and Muir, 2005). Pain perception involves a transduction of chemical signals into electrical signals at the site of injury, followed by transmission of such signals through nerve fibers up to the spinothalamic tracts where modulation may occur in the dorsal horn or continued to the brain for perception (Muir and Woolf, 2001). Pain due to surgery involves an immediate incisional response and a latent response due to inflammation and tissue damage (Kissin, 2000). The purpose of pre-surgical analgesia is to alleviate the incisional and inflammatory responses involved in the pain process. This could be achieved through multimodal analgesic strategies such as a combination of local anesthetic and sedative analgesic agents (opioids) in order to act on different receptor targets along the nociceptive pathway resulting into improved perioperative analgesia (Muir and Woolf, 2001).

Loco-regional anesthesia is favored in small ruminants over general anesthesia due to less equipment needed and to avoid the risk of bloating and regurgitation associated with placing the animal in recumbency (Galatos, 2011). Epidural anesthesia is a common loco-regional anesthetic technique in small ruminant surgery owing to feasibility, low cost, specific regional blockade and rapid recovery (Abrahamsen, 2008). Lidocaine, mepivacaine and bupivacaine are local anesthetic agents commonly used for epidural analgesia in small ruminants. Lidocaine and mepivacaine are short acting anesthetics and re-administration might be necessary during the procedure (Lomax et al., 2009). Bupivacaine is a long acting local anesthetic characterized by prolonged analgesia and motor disturbances (DeRossi et al., 2012). Epidural analgesia through injection of an opioid is a widely used technique in veterinary practice to overcome the motor blockade caused by the local anesthetic agents (Abrahamsen, 2008). Butorphanol is a synthetic opioid that possesses about 5 times analgesic potency as morphine and fewer negative effects on the gastrointestinal and respiratory tracts compared with morphine (Carroll et al., 2001).

Combination of local anesthetics and opioids aims to provide better analgesia and reduce the undesirable side effects. Epidural analgesia using combinations of tramadol-lignocaine (Ajadi et al., 2012; Dehkordi et al., 2012), lidocaine-butraphanol (Turi et al., 2018) and bupivacaine-methadone (DeRossi et al., 2015) have been reported in goats; however, epidural butorphanol or butorphanol-bupivacaine combination were not used in goats. Therefore, the objective of the present study was to evaluate the analgesic effect of lumbosacral epidural administration of bupivacaine, butorphanol and butorphanol-bupivacaine combination in goats.

2. Materials and methods

Fifteen adult non-pregnant female goats, aged between 2 - 5 years (mean 3 ± 0.95 years) and weighing 28 - 40 kg (mean 33.27 ± 3.52 kg), were enrolled in this study. Animals were subjected to thorough clinical, blood and parasitic examinations according to Radostits et al. (2000) and Soulsby (1968) respectively, and selected goats were approved to be apparently healthy and free from infectious diseases as well as external and internal parasites. Fresh clean tap water was available ad libitum along the day before undergoing epidural anesthesia and food was withheld for 12 hrs. prior to the experiment. Animals were randomly divided into three equal groups (A, B and C) consisting of 5 animals. Animals of group A were administered epidural bupivacaine HCL 0.5 % (Markyrene® Sigma-Tec pharmaceutical Indust.Co) in a dose rate of 0.5 mg/kg bodyweight. In group B, butorphanol tartrate 1 % (Torbugesic® Zoetis Australia Pty Ltd) was epidurally administered in a dose rate of 0.08 mg/kg bodyweight and bupivacaine HCL 0.5 % in a dose rate of 0.25 mg/kg bodyweight. Butorphanol tartrate 1 % in a dose rate of 0.04 mg/kg bodyweight was epidurally injected in group C.

For each trial, the lumbosacral region was clipped and prepared for aseptic epidural puncture. An 18-gauge needle was inserted into the lumbosacral epidural space at the intervertebral depression between the last lumbar and first sacral vertebrae. Correct needle placement into the epidural space was confirmed by hanging drop test and/or absence of resistance during injection. The calculated dose for

each animal in each group was equalized to 5 mL using sterile water and slowly injected. Animals were kept in a clam quiet place provided with soft straw bedding during the study.

Analgesia, sedation, and motor effects were assessed according to Singh et al., (2007) by an observer who was blind to the injected drug (Table 1).

Table (1): Description of analgesia, degree of ataxia and sedation scores.

Score	Analgesia score	Degree of ataxia	Sedation score
0	No analgesia	Normal gait	Standing alert
1	Mild analgesia weak or depressed response	Slight stumbling and able to continue walking	Standing but tired with slight ptosis of eyelids
2	Moderate analgesia no response to superficial skin pricks	Marked stumbling, walking but very ataxic	Standing with wide stance and lowering of head
3	Complete analgesia (no response to deep muscle pricks)	Sternal recumbency	Animal attained recumbency but could sit without support
4	----------	Lateral recumbency	Lateral recumbency

The onset (time elapsed from injection to loss of sensation), duration (time between loss and reappearance of response), and anatomic distribution (tail, perineum, and inguinal region) of analgesia were recorded for all groups. The onset of analgesia was recorded by pinprick method (Aithal et al., 1996) at the perineal region every minute interval until a response was observed then at 10 minutes intervals until a response reoccurred. Positive responses to the stimuli were defined as purposeful avoidance movement of head, neck, trunk, limbs, tail; contracture of the anus, and/or turning of the head toward the stimulation site. The degree of ataxia and sedation scores was evaluated every 10 minutes till the end of the study.

Physiological parameters including heart rate, respiratory rate, and rectal temperature were assessed at baseline (time 0) and at 15-minute interval after injection till the end of the study according to Radostits et al. (2000).

Statistical analysis

Data were analyzed using SPSS program (SPSS for windows Version 16, SPSS Inc., Chicago, USA). Kolmogorov–Smirnov test was used to assure the normal distribution of the obtained data. Statistically significant differences between groups were determined by analysis of variance (ANOVA). When the differences were significant, Duncan's multiple range test was performed. Mean values were considered significantly different at ($P < 0.05$). Data are expressed as (mean values ± SD).

3. Results

Epidural administration of various agents was safely performed without complications and the bupivacaine and butorphanol solutions were miscible. When positive results for the hanging drop technique were not evident or there was resistance to injection, the needle was withdrawn and reintroduced. Prior injection, aspiration was performed and blood was never withdrawn from the epidural needle.

The onset of analgesia was significantly ($P < 0.05$) earlier in the butorphanol group (9.8 ± 1.1 Min) than the butorphanol-bupivacaine group (12.8 ± 0.84 Min) and bupivacaine group (16.6 ± 0.55 Min). The duration of analgesia was significantly ($P < 0.05$) longer in the Butorphanol-bupivacaine group (208.4 ± 8.36 Min) than the butorphanol (166 ± 5.48 Min) and bupivacaine (112 ± 8.37 Min) groups (Table 2).

Table (2): Onset and duration of analgesia:

Group	Onset	Duration
(A)	16.60 ± 0.55^{c}	112.00 ± 8.37^{a}
(B)	9.80 ± 1.10^{a}	166.00 ± 5.48^{b}
(C)	12.80 ± 0.84^{b}	208.00 ± 8.37^{c}
F	79.18	204.35
P-value	*< 0.001***	*< 0.001***

Means with different superscript letters are statistically different at $P < 0.05$

In figure (1), it was clear that animals in all groups received an analgesia score of 0 (no analgesia) at baseline with an intense response and fast reaction to

the noxious stimulus (pin prick). Distribution of analgesia in the tail, perineum and inguinal regions was similar in all groups. However, butorphanol-bupivacaine combination produced profound analgesia (no response to deep muscular pricks) that was evident by higher long lasting (from the 30th to the 170th Min) analgesia scores compared to the bupivacaine and butorphanol groups.

The degree of ataxia was illustrated in Fig. 2.The bupivacaine group showed mild degree of ataxia (score = 1) up to 30 minutes, then animals showed sternal recumbency (score = 3) from the 50th to 80th minute post epidural administration. After almost one and half hour post anesthetic administration, animals started to exhibit lower scores (1) of ataxia. In the bupivacaine-butorphanol group three goats received an ataxia score of 1. The other two goats had a score of 0 for 30 minutes, and then at the 40th minute they had an ataxia score of 1. Goats had difficulty moving but managed to remain standing without help. Sternal recumbency was not encountered in the bupivacaine-butorphanol group. Goats of the butorphanol group presented an ataxia score of 0 throughout the study showing no motor disturbances.

Twenty minutes post-epidural administration of butorphanol, goats (4/5) exhibited signs of sedation (score = 1) then at the 30th minute all animals (5/5) showed signs of sedation that was evidenced by slight dropping of the upper eyelid. Moderate sedation with lowering of the head was seen in the butorphanol group from the 60th to the 100th minute then sedation scores decreased. In the butorphanol-bupivacaine group, two animals showed signs of mild sedation at the 30th minute post-epidural injection. At the 40th minute, all animals in the group became mildly sedated (score = 1) up to the 170th minute, then sedation scores decreased. None of the butorphanol-bupivacaine group showed moderate sedation scores (2). Animals of the bupivacaine group were alert during the experiment with a sedation score of 0 and signs of sedation were not observed (Fig. 3).

Assessment of the physiological parameters revealed significant increase in heart rate in the butorphanol and butorphanol-bupivacine groups compared to base line, although it was within normal limit. The respiratory rate and rectal temperature showed no significant differences in relation to any of the parameters when compared to baseline, or between each other (Table 3).

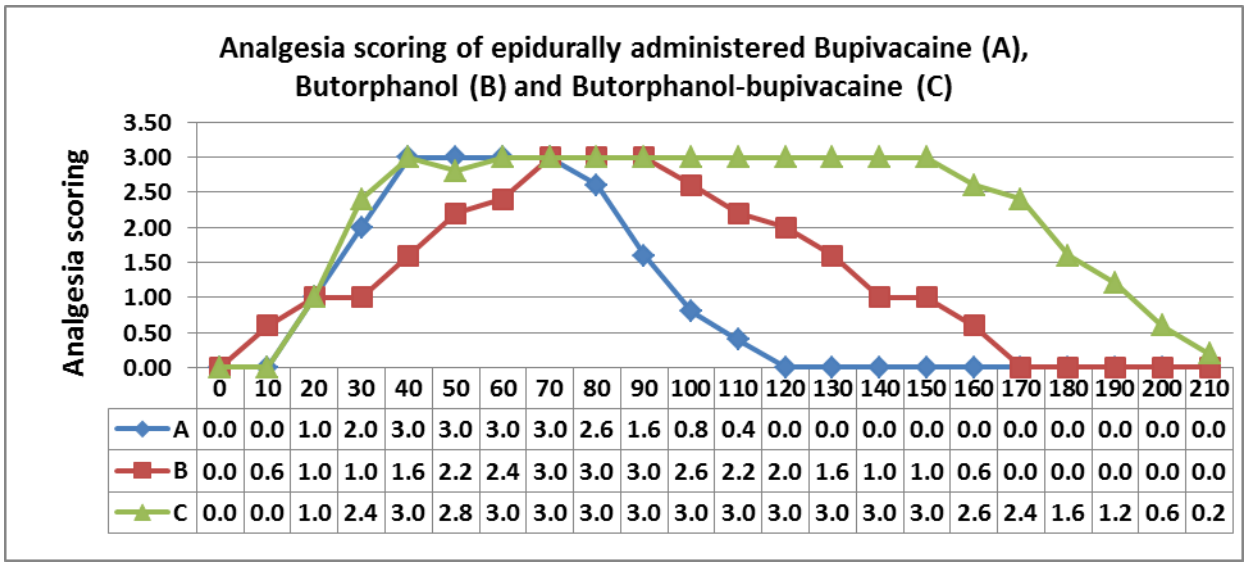
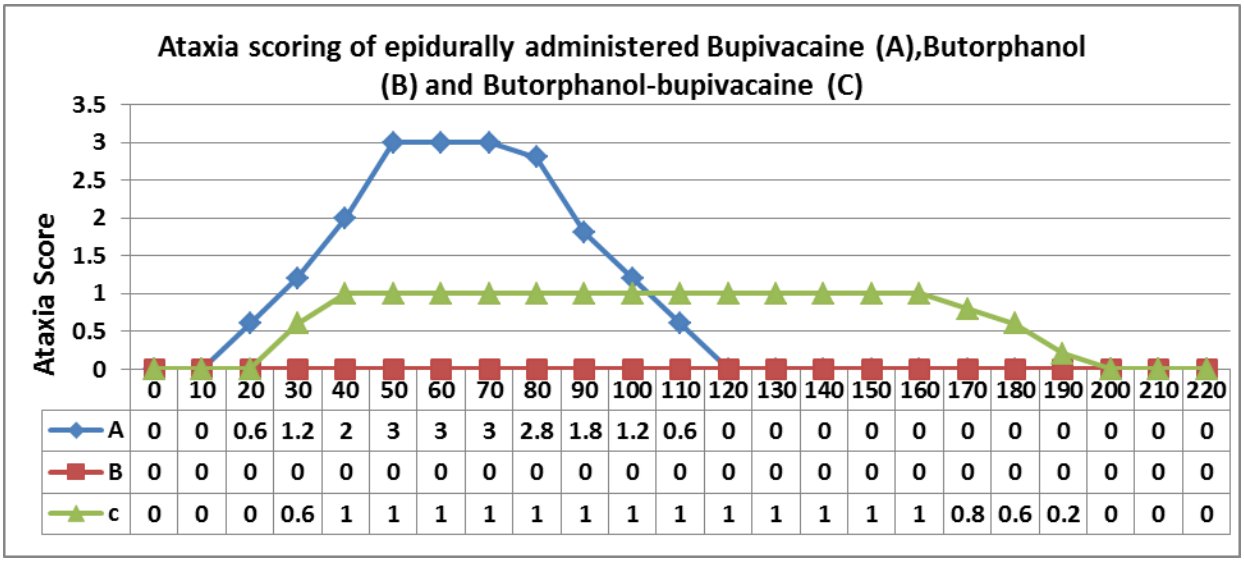
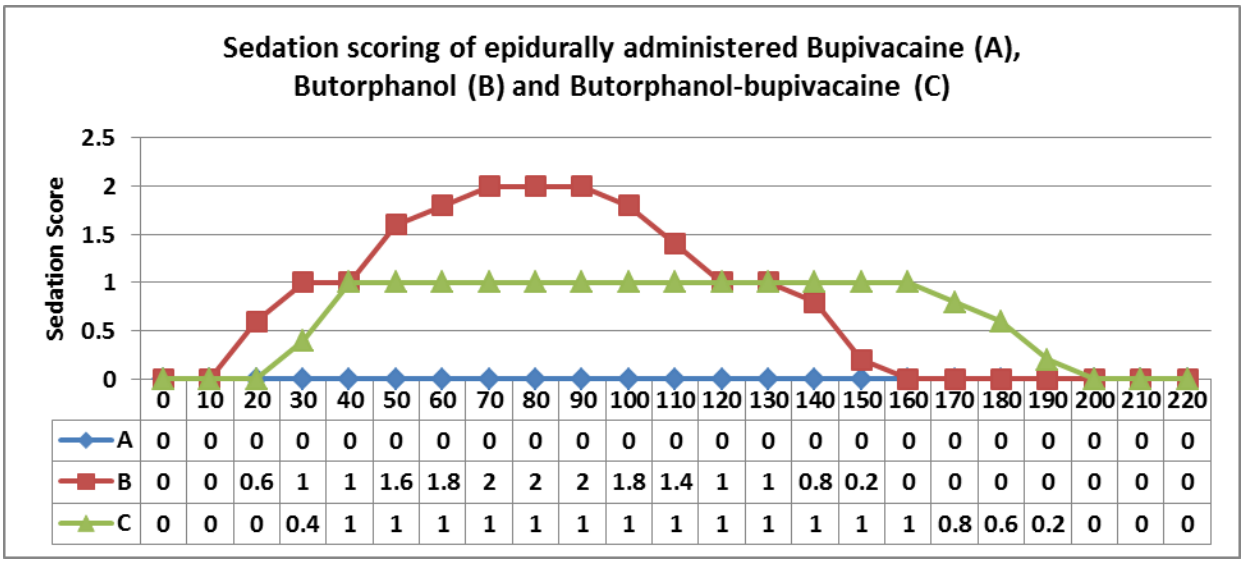


Fig. 1. Analgesia scoring of epidurally administered Bupivacaine (A), Butorphanol (B) and Butorphanol-bupivacaine (C) groups over the duration.



	0	10	20	30	40	50	60	70	80	90	100	110	120	130	140	150	160	170	180	190	200	210	220
A	0	0	0.6	1.2	2	3	3	3	2.8	1.8	1.2	0.6	0	0	0	0	0	0	0	0	0	0	0
B	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
c	0	0	0	0.6	1	1	1	1	1	1	1	1	1	1	1	1	1	0.8	0.6	0.2	0	0	0

Fig. 2. Ataxia scoring of epidurally administered Bupivacaine (A), Butorphanol (B) and Butorphanol-bupivacaine (C) groups over the duration.



	0	10	20	30	40	50	60	70	80	90	100	110	120	130	140	150	160	170	180	190	200	210	220
A	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
B	0	0	0.6	1	1	1.6	1.8	2	2	2	1.8	1.4	1	1	0.8	0.2	0	0	0	0	0	0	0
C	0	0	0	0.4	1	1	1	1	1	1	1	1	1	1	1	1	1	0.8	0.6	0.2	0	0	0

Fig. 3. Sedation scoring of epidurally administered Bupivacaine (A), Butorphanol (B) and Butorphanol-bupivacaine (C) groups over the duration.

Table 3: Mean values ± standard deviation of heart rate (HR), respiratory rate (RR), and rectal temperature (RT) of Bupivacaine (A), Butorphanol (B) and Butorphanol-bupivacaine (C) groups over the study duration.

Time (Min)	Heart Rate (beat/min)			Respiratory Rate (breath/min)			Rectal Temperature (°C)		
	(A)	(B)	(C)	(A)	(B)	(C)	(A)	(B)	(C)
0	74.00 ±2.45^{a}	76.40 ±2.61^{a}	80.80 ±3.35^{b}	18.40 ±2.61	18.80 ±3.35	21.20 ±2.28	39.30 ±0.24	39.32 ±0.22	39.32 ±0.22
15	83.20 ±3.90^{b}	78.80 ±2.28^{a}	85.60 ±2.61^{b}	22.40 ±4.77	19.20 ±3.03	24.40 ±1.67	39.18 ±0.11	39.22 ±0.15	39.32 ±0.22
30	81.60 ±4.56^{ab}	76.80 ±3.03^{a}	83.60 ±2.97^{b}	22.00 ±3.16^{b}	18.40 ±2.61^{a}	23.20 ±1.10^{b}	39.12 ±0.11	39.20 ±0.12	39.18 ±0.16
45	79.60 ±4.10^{b}	74.80 ±3.35^{a}	81.60 ±2.19^{b}	21.20 ±3.63	18.00 ±2.45	20.80 ±1.10	39.10 ±0.22	39.18 ±0.11	39.12 ±0.15
60	76.80 ±4.15	76.40 ±6.54	80.00 ±2.45	20.00 ±3.16	17.60 ±2.61	20.40 ±0.89	39.10 ±0.22	39.16 ±0.11	39.10 ±0.12
75	76.40 ±3.29^{b}	71.60 ±0.89^{a}	78.40 ±1.67^{b}	18.40 ±2.61^{ab}	16.40 ±0.89^{a}	19.60 ±0.89^{b}	39.10 ±0.22	39.18 ±0.13	39.12 ±0.15
90	74.80 ±3.03^{b}	71.60 ±0.89^{a}	77.60 ±2.19^{b}	18.40 ±2.61	16.40 ±0.89	18.40 ±0.89	39.10 ±0.22	39.20 ±0.12	39.10 ±0.12
105	74.40 ±2.19^{b}	70.80 ±1.10^{a}	75.60 ±1.67^{b}	18.40 ±2.61	16.40 ±0.89	16.80 ±1.10	39.10 ±0.22	39.18 ±0.11	39.10 ±0.11
120	74.00 ±2.45^{b}	70.40 ±0.89^{a}	75.20 ±1.79^{b}	18.40 ±2.61	16.40 ±0.89	16.80 ±1.10	39.22 ±0.30	39.16 ±0.15	39.18 ±0.16
135	76.90 ±2.15	72.00 ±1.60	74.00 ±1.41	18.20 ±3.41	18.00 ±2.45	16.00 ±0.89	39.40 ±0.14	39.00 ±0.11	39.12 ±0.15
150	76.40 ±1.29	74.00 ±1.41	74.00 ±1.41	22.10 ±4.77	18.00 ±2.45	16.80 ±1.10	39.18 ±0.11	39.20 ±0.12	39.12 ±0.15
165	76.60 ±3.56	75.20 ±2.28	74.00 ±1.41	18.40 ±2.51	18.00 ±2.45	18.80 ±1.10	39.15 ±0.11	39.18 ±0.13	39.12 ±0.15
180	79.60 ±2.10	76.00 ±2.00	72.80 ±2.68	19.50 ±1.51	18.00 ±2.45	20.40 ±2.61	39.11 ±0.21	39.20 ±0.12	39.12 ±0.15
195	76.80 ±3.15	76.30 ±3.21	72.80 ±2.68	22.00 ±2.61	17.60 ±2.61	20.80 ±2.28	39.12 ±0.25	39.17 ±0.14	39.32 ±0.22
210	75.60± 2.56	77.40 ±2.61	72.80± 2.68	20.30 ±3.61	17.40 ±0.79	20.80 ±2.28	39.18 ±0.11	39.18 ±0.15	39.32 ±0.22

Means with different superscripts letters in the same column are significantly different at $p < 0.05$

4. Discussion

The present study is the first to investigate the effects of epidural administration of butorphanol alone or in combination with bupivacaine in goats. Epidural administration of butorphanol-lidocaine combination was recorded in goats (Turi et al., 2018); however, the use of butorphanol alone or in combination with bupivacaine for epidural analgesia in goat has not been reported. The recommended dose of butorphanol in our study was extrapolated from previous studies in goat (Turi et al., 2018) and horse (Natalini and Robinson, 2000). The dose of bupivacaine was selected according to a previous study in goat (Singh et al., 2007). Bupivacaine is a highly lipophilic local anesthetic agent, has a potency of four times as lidocaine and longer duration (Butterworth, 2009). Combination of bupivacaine and opioids has demonstrated satisfactory results in small ruminants (DeRossi et al., 2012; DeRossi et al., 2015). Similar findings were observed in our study, where epidural injection of butorphanol-bupivacaine combination has provided better perioperative analgesia characterized by faster pain relief (than bupivacaine), longer duration and improved quality (than bupivacaine or butorphanol) and eliminates the adverse motor effects of bupivacaine.

Butorphanol is a synthetic, lipid-soluble opioid with a strong kappa-receptor agonist activity. Kappa-receptors are involved in the somatic and visceral pain modulation, so it is useful in reducing postoperative pain (Waterman et al., 1991). The analgesic effects of epidural administration of opioids are due to diffusion of the drug through meninges to the spinal cord then binds to opioid receptors in the dorsal horn that are involved in the signal processing of nociception. This results into segmental spinal analgesia of long duration without motor paralysis (Smith and Yu JK, 2001). This is consistent with our results, where the duration of butorphanol alone or in combination with bupivacaine was longer than the duration of bupivacaine. Similar findings were reported in human (Bharti and Chari, 2009) and horse (Natalini and Robinson, 2000). The rapid onset of analgesia in the butorphanol group and butorphanol-bupivacaine group compared to the bupivacaine group may be attributed to the high lipid solubility, molecular size and faster penetration of butorphanol into the spinal canal (Smith and Yu JK, 2001).

In the current study, combination of butorphanol and bupivacaine improved the quality of analgesia compared to the use of either bupivacaine or butorphanol alone. This may be attributed to the mechanism of action of each agent in blocking nerve impulses. Butorphanol inhibits the synaptic pain-impulse transmission through inhibition of substance P release from the primary afferent neurons and on postsynaptic opioid receptors to hyperpolarize the transmission cells. Bupivacaine acts primarily by inhibition of action potentials via sodium channel blockade (Saxena and Arava, 2004). These compounds may act synergistically and are therefore increasingly co-administered.

The locomotor disturbances observed in the bupivacaine group and mild ataxia in the bupivacaine-butorphanol group could be due to the sensory and motor block produced by bupivacaine (Day and Skarda, 1991). Sedation observed in the butorphanol and bupivacaine–butorphanol combination groups may be due to systemic effects of the absorbed butorphanol to blood stream.

The main advantage of butorphanol is its fewer side effects. High lipid solubility and high affinity for opioid receptors are additional factors that contribute to the paucity of side effects with butorphanol. High lipid solubility increases diffusion in the spinal cord and limits the amount of drugs remaining in the cerebrospinal fluid capable of reaching the brainstem, where side effects occur (thermoregulatory, cardiac and respiratory centers). In the present study, heart rate was significantly ($P < 0.05$) increased from base line in the butorphanol and butorphanol-bupivacine groups; however, it was within normal limit. Similar increase in heart rate was reported following epidural administration of opioids and may be attributed to serotonin syndrome which causes increase of heart rate and blood pressure (Cossman and Wilsmann, 1987). The respiratory rate and rectal temperature were not changed significantly from base line in all groups. Similar findings were recorded in human (Bharti and Chari, 2009) and goats (dos Santos Silva et al., 2017).

In conclusion, butorphanol alone produces analgesia of long duration but of slow onset. The combination of bupivacaine–butorphanol administered epidurally in goat resulted into rapid onset and prolonged duration of analgesia. The obtained results suggest that bupivacaine–butorphanol combination could be used efficiently for surgical interventions and obstetrical procedures that require long duration and effective analgesia.

5. References

Abrahamsen EJ (2008). Ruminant field anesthesia. Vet. Clin. North. Am. Food Anim. Pract., 24(3): 429-41

Aithal HP, Amarpal, Pratap K, Singh GR (1996). Clinical effects of epidurally administered ketamine and xylazine in goats. Small Ruminant Res. 24, 55–64.

Ajadi RA, Owanikin AO, Martins MM, Gazal OS (2012). Effect of epidural tramadol and lignocaine on physiological and behavioral changes in goats subjected to castration with a high tension band. New Zeland Vet. J., 60(6): 344-348.

Anderson DE, Muir WW (2005). Pain management in ruminants. Vet. Clin. North. Am. Food Anim. Pract., 21: 19–31.

Bharti N, Chari P (2009). Epidural butorphanol-bupivacaine analgesia for postoperative pain relief after abdominal hysterectomy. J. Clin. Anesth., 21(1): 19-22.

Butterworth JF (2009). Clinical pharmacology of local anesthetics. In: Cousins MJ, Carr DB, Horlocker TT, Bridenbaugh, eds. Cousins & Bridenbaugh's Neural Blockade in Clinical Anesthesia and Pain Medicine, 4th edn. Philadelphia: Lippincott Williams & Wilkins, 96–113.

Carroll GL, Boothe DM, Hartsfield SM, Waller MK, Geller SC (2001). Pharmacokinetics and selected behavioral responses to butorphanol and its metabolites in goats following intravenous and intramuscular administration. Vet. Anaesth. Analg., 28(4): 188-195.

Cossman M, Wilsmann KM (1978). Effect and side effects of tramadol: an open phase IV study with 7198 patients. Therapiewoche, 37: 3475–85.

Day TK, Skarda RT (1991). The pharmacology of local anesthetics. Vet. Clin. North. Am. Equine Pract., 7, 489–500.

Dehkordi SH, Bigham AS, Gerami R (2012). Evaluation of anti-nociceptive effect of epidural tramadol, tramadol lidocaine and lidocaine in goats. Vet. Anesth. Analg., 39: 106–110.

DeRossi R, Jardim P, Hermeto L, Pagliosa R (2015). Comparison of analgesic and systemic effects of bupivacaine, methadone, or bupivacaine/methadone administered epidurally in conscious sheep. Aust. Vet. J., 93: 164–169.

DeRossi R, Pagliosa R, Módolo TC, Maciel FB, Macedo GG (2012). Thoracic epidural analgesia via the lumbosacral approach using multiport catheters with a low concentration of bupivacaine and morphine in sheep. Vet. Anaesth. Analg., 39(3): 306-314.

Dos Santos Silva P, Fantinato-Neto P, Silva ANE, Junior EHB, Carregaro AB (2017). Thoracolumbar epidural anaesthesia with 0.5% bupivacaine with or without methadone in goats. Ir. Vet. J., 26; 70:15.

Galatos AD (2011). Anesthesia and analgesia in sheep and goats. Vet. Clin. North. Am. Food Anim. Pract., 27(1): 47-59.

Kissin I (2000). Preemptive analgesia. Anesthesiology, 93: 1138–1143.

Lomax S, Sheil M, Windsor PA (2009). Use of local anaesthesia for pain management during husbandry procedures in Australian sheep flocks. Small Rumin. Res. 86: 56–58.

Monteiro ER, Adolfo RJ, Assis HM, Campagnol D, Quitzan JG (2009) Comparative study on the sedative effects of morphine, methadone, butorphanol or tramadol, in combination with acepromazine in dogs. Vet. Anaesth. Analg., 36, 25-33.

Muir WW, Woolf CL (2001). Mechanisms of pain and their therapeutic implications. J. Am. Vet. Med. Assoc., 219(10): 1346–1156.

Natalini CC, Robinson EP (2000). Evaluation of the analgesic effects of epidurally administered morphine, alfentanil, butorphanol, tramadol, and U50488H in horses. Am. J. Vet. Res., 61(12): 1579-1586.

Radostits, O. M., Mayhew, I.G. and Houston, D. M. (2000). Veterinary clinical examination and diagnosis. Harcourt Publisher Limited, W. R. Saunders, London.

Rollin BE (2004). Annual meeting keynote address: animal agriculture and emerging social ethics for animals. J. Anim. Sci. 82: 955–964.

Saxena AK, Arava SK (2004). Current concepts in neuraxial administration of opioids and non-opioids: an overview and future perspectives. Indian J. Anaesth., 48: 13–24.

Singh K, , Kinjavdekar P, Amarpa, Aithal HP, Gopinathan A, Singh GR, Pawde AM, Pratap K (2007). Comparison of the analgesic, clinicophysiological and hematobiochemical effects of epidural bupivacaine in healthy and uremic goats. Small Rum. Res., 71: 13–20

Smith LJ, Yu JK (2001). A comparison of epidural buprenorphine with epidural morphine for postoperative analgesia following stifle surgery in dogs. Vet. Anaesth. Analg., 28(2): 87-96.

Soulsby, EJL (1968). Helminthes, Arthropods and Protozoa of domesticated animals. (6th Edition of Monining, Veterinary Helminthology and Entomology) London Bailliere, TIDALL and Gassal.

Turi D, Sharma AK, Gupta MK, Roy KB (2018). Anaesthetic evaluation of lignocaine alone and in-combination with butorphanol in goats. Indian J. Anim. Res., 52 (3): 409-412.

Waterman AE, Livingston A, Amin A (1991). Analgesic activity and respiratory effects of butorphanol in sheep. Res. Vet. Sci., 51:19.