The effects of adding epinephrine or xylazine to lidocaine solution for lumbosacral epidural analgesia in fat-tailed sheep

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This blinded, randomised experimental study was designed to compare the analgesic effects of lumbosacral epidural administration of lidocaine-epinephrine or lidocaine-xylazine combinations in fat-tailed sheep. Nine healthy fat-tailed male lambs (mean ± s.d. age, 4.6 ± 0.4 months; weight, 24.6 kg ± 2.5 kg) were randomly allocated into four groups of six sheep: lidocaine 2% (LID), lidocaine-epinephrine 5 µg/mL (LIDEP), lidocaine-xylazine 0.05 mg/kg (LIDXY) or bupivacaine 0.5% (BUP). The onset and duration of flank, perineum and hindlimb anaesthesia and the onset and duration of hindlimb paralysis were recorded. Epidural administration of LID, LIDEP, LIDXY or BUP produced anaesthesia within 6.6 min, 7.6 min, 3.4 min and 8.4 min, respectively. The mean onset of anaesthesia in the LIDXY group was significantly shorter compared with the BUP group ($p = 0.02$). The mean duration of anaesthesia was 107.9 min, 190.4 min, 147.6 min and 169.7 min for LID, LIDEP, LIDXY and BUP, respectively. The onset of hindlimb paralysis was faster in the LIDXY group than in the BUP group; however, the duration of hindlimb paralysis was shorter in LIDXY compared with LIDEP. Epidural administration of LIDEP or LIDXY provides a comparable duration of local anaesthesia without any adverse effects in fat-tailed sheep. Epidural LIDXY did not appear to be advantageous over epidural LIDEP.

Introduction

Surgical procedures in ruminants are usually performed under local or regional anaesthesia. Lumbosacral (L6-S1) epidural anaesthesia is the most common epidural technique used in sheep, goats and calves for all procedures caudal to the umbilicus.[1,2] Lidocaine is the most frequently used local anaesthetic solution for epidural or subarachnoid anaesthesia in small ruminants, which causes a blockage of the sensory, sympathetic and motor fibres, producing hypotension and ataxia.[3] Longer lasting local anaesthetics, for example, bupivacaine, can be used epidurally to provide postoperative analgesia as well.[4,5,6,7] Bupivacaine is approximately four times as potent as lidocaine and provides a longer duration of anaesthesia with a slower onset of action.[3]

Two major groups of drugs are used to increase the depth or duration of local anaesthetics for epidural block: vasoconstrictors (mainly epinephrine) and alpha$_2$-adrenergic agonists. Xylazine is an alpha$_2$-adrenoceptor agonist that is used as a sedative in veterinary practice. It appears to exhibit direct local anaesthetic sensory and motor nerve blocking actions in addition to its spinal cord alpha$_2$-adrenoceptor-mediated analgesic effects.[2] The alpha$_2$-agonists can be absorbed from the epidural space and have systemic effects (sedation and cardiopulmonary depression) that are most obvious in the ruminants because of their increased sensitivity to this group of drugs.[8] Xylazine alone, or in combination with lidocaine, has been used for epidural or subarachnoid anaesthesia in a variety of species and it has been demonstrated that their combination induces a more prolonged analgesia than that observed with the use of either drug alone.[9,10,11,12,13,14,15] In these studies, a lidocaine-xylazine combination has been compared with lidocaine alone.

To our knowledge, a direct comparison of the effect of epinephrine or xylazine addition on the anaesthetic properties of lidocaine after epidural administration has not been reported previously. Therefore, the objective of the study reported here was to evaluate the analgesic efficacy of lidocaine-epinephrine or lidocaine-xylazine combinations following lumbosacral epidural administration in fat-tailed sheep. Lidocaine and bupivacaine groups have been included for comparison.

Materials and methods

Nine healthy, 4–5-month-old (mean ± s.d., 4.6 ± 0.4 months; range 4.3–5.3 months), fat-tailed Mehraban male lambs, with a body condition score of 3.3 ± 0.3 (range 3–3.5; on a scale of

0–5 units[16]) and with a mean (± s.d.) weight of 24.6 ± 2.5 kg (range 21 kg – 27 kg) were used in the present study. Six sheep were used on three occasions and three sheep were used twice.

The sheep were confined to indoor pens and were given alfalfa, concentrate (grain mix) and water *ad libitum* and were allowed an acclimation period of 2 weeks prior to the beginning of the study. Their health status was established on the basis of a thorough physical examination and normal complete blood count and total protein. A faecal sample examination revealed no parasite infestation. Sheep were randomly assigned to one of four groups (six sheep per group) and received either 2% lidocaine hydrochloride (LID) (Caspian Tamin Pharmaceutical Co., Rasht, Iran), 2% lidocaine hydrochloride with 5 µg/mL epinephrine (LIDEP) (Darou Pakhsh Co., Tehran, Iran), 2% lidocaine hydrochloride with 0.05 mg/kg xylazine (LIDXY) (Alfasan, Woerden, the Netherlands) or 0.5% bupivacaine hydrochloride (BUP) (Merk Company, Lyon Cedex, France), with at least a 7-day interval between experiments. Lidocaine-epinephrine and lidocaine-xylazine solutions were freshly prepared by adding epinephrine (1:1000) or xylazine (2%) to 2% lidocaine, immediately before use. The pH of the anaesthetic solutions was measured using a pH meter (Crison, Basic 20+).

Animals were fasted for 12 h before the experiment, but water was available for them at all times. Skin overlaying the lumbosacral area was prepared aseptically before placement of an epidural needle. After locating the lumbosacral intervertebral space, 1 mL of local anaesthetic solution was injected using a 22-gauge needle to desensitise the skin and subcutaneous tissue. A 3 cm 16-gauge needle was used as a cannula, minimising skin resistance during the insertion of a 9 cm 19-gauge Tuohy needle (IMS, Tokyo, Japan) through a dorsal midline approach. When the needle tip reached the ligamentum flavum, the stylet was removed and a glass syringe was attached to the hub of the needle. The needle was then inserted slowly into the epidural space with the bevel directed cranially. Entrance into the epidural space was identified by means of the loss of resistance to air injection. After aspiration of the needle to confirm that there was no blood or CSF present, the anaesthetic solution was administered. All drugs were administered slowly over approximately 30 s in each sheep.

The anaesthetic solution consisted of 5 mL of LID, LIDEP, LIDXY or BUP for each epidural block; therefore, all sheep received a fixed total volume of 5 mL of anaesthetic solution. The distance from the skin to the epidural space was determined by measuring the length of the needle (distance between the needle hub and tip of the needle) and subtracting the distance between the skin and needle hub. Following the administration of the anaesthetic solution, the needle was removed and the sheep was placed in a canvas sling in a standing position.

Both the time to the onset and the duration of complete anaesthesia in the flank, perineum and hindlimb was recorded, based on the complete absence of response to painful stimuli including superficial and deep pin pricks with a 25-gauge needle and the pinching of skin with haemostats closed to the first ratchet. The onset and duration of hindlimb paralysis were also determined by flexing the hindlimbs manually to evaluate muscle tone and the animal's ability to support its own weight. In order to determine the time to onset, analgesic testing was performed every 30 s after the completion of the epidural injection. Anaesthesia was evaluated every 10 min until a response was observed. To avoid any bias or potential manipulation of data, the same investigator assessed the anaesthesia in all cases and was unaware of the treatment given.

The arterial haemoglobin-oxygen saturation (SaO_2) was measured through a pulse oximetry sensor (Pulse Oximeter, Oxicap 425, Soor Afarinesh Bartar Co., Tehran, Iran) attached to the ear, which was previously shaved. Heart rate (HR) was measured by counting the heart beats over the cardiac area using a stethoscope. The electrocardiogram was monitored using a bas-apex lead with paper speed and sensitivity of 25 mm/sec and 10 mm/mV, respectively (Kenz ECG 110, Suzuken Co. LTD, Nagoya, Japan). Respiratory rate (RR) was measured by counting chest movements per minute and rectal temperature (RT) was measured with a digital thermometer. HR, RR and RT were measured before epidural drug administration (time 0) and at 5 min, 10 min, 15 min, 20 min, 30 min, 40 min, 50 min, 60 min and 75 min after the drug injection and, thereafter, every 15 min until the end of anaesthesia.

All data are presented as mean ± s.d. for each treatment group. HR, RR and RT values were compared using analysis of variance (ANOVA) for repeated-measures, with time and group as factors, followed by Duncan's test. A one-way ANOVA followed by Duncan's test was used to compare the onset and duration of anaesthesia, as well as the distance from the skin to the epidural space. Statistical analysis was undertaken using SPSS Version 10 for Windows (SPSS, MicroMaster, Richboro, PA, USA) and $p \leq 0.05$ was considered significant.

Ethical considerations

The Institutional Animal Care and Use Committee approved the protocol for this project.

Results

There were no significant differences in body weight between the four groups of sheep (Table 1). No difficulty was encountered in locating the proper site for injection of the local anaesthetic. The procedure for each sheep was completed within 5 min and was well tolerated by all experimental animals. The mean distance from the skin to the epidural space was 3.4 ± 0.3 cm (range 3.0 cm – 3.9 cm). The doses of lidocaine in the LID, LIDEP and LIDXY groups

were 5.0 ± 0.6 mg/kg, 5.1 ± 0.5 mg/kg and 4.8 ± 0.4 mg/kg, respectively. The mean dose of bupivacaine in BUP group was 1.2 ± 0.1 mg/kg.

Significant difference was not detected between groups in time to the onset of anaesthesia for the flank and perineum, but the onset of hindlimb anaesthesia for both LID and LIDXY treatments was significantly faster ($p < 0.05$) than that for BUP (Table 1). The onset of hindlimb anaesthesia was also faster following LIDXY treatment compared to that of LIDEP. Ataxia and hindlimb paralysis were observed in all groups and sheep became recumbent within 15 min. The onset of hindlimb paralysis was significantly longer in the BUP group compared with that of LIDXY. The duration of anaesthesia for the flank was significantly longer ($p < 0.05$) in the LIDEP and BUP groups compared with that of LID (Figure 1). The mean duration of anaesthesia in the perineum, flank and hindlimb after epidural administration of LIDEP, LIDXY and BUP were 190.4 min ± 51.1 min, 147.6 min ± 24.3 min and 169.7 min ± 57.2 min, respectively. The mean duration of anaesthesia in the LID group (107.9 min ± 39.0 min) was significantly shorter than that of LIDEP ($p < 0.05$). The onset of hindlimb paralysis was faster in sheep in the LIDXY group (3.5 min ± 2.1 min) than in sheep in the BUP group (10.5 min ± 5.0 min) (Table 1); however, the duration of hindlimb paralysis was shorter in LIDXY (91.5 min ± 25.6 min) compared to LIDEP (146.2 min ± 48.9 min) (Figure 1).

No change in HR was observed in the LID, LIDXY and BUP groups; however, overall HR was lower with the LIDXY treatment. HR decreased to 55 beats/min and sporadic ventricular premature beats were observed in one sheep receiving LIDXY. In the LIDEP group, a significant increase in HR occurred 15 min after epidural administration (Figure 2). A slight reduction in RR and RT in all four groups was deemed insignificant (Figures 3 and 4). Arterial haemoglobin-oxygen saturation was within clinically acceptable limits and was not different between groups. Mild sedation (drowsiness and a slight drooping of the head) and frequent urination were observed in the LIDXY group. The pH of LID, LIDEP, LIDXY and BUP was 6.28, 6.27, 6.26 and 5.56, respectively. No toxic or adverse neurological reactions associated with epidural administration of any of the solutions or obvious signs of systemic toxicity (extensor rigidity, muscle twitching and convulsions) were encountered after performing the epidural block in any of the sheep in this study.

Discussion

Local anaesthetics have the ability to block the sensation of pain completely and have been used clinically as adjuncts to light general anaesthesia in both small and large animals.[3] They decrease general anaesthetic requirements, improve the quality of recovery and prevent central sensitisation of the nociceptive pathway after painful surgical procedures, reducing the requirements for postoperative analgesia.[17] Local and regional anaesthetic techniques may be used before, during, or after surgery to provide intra-operative and postoperative analgesia.

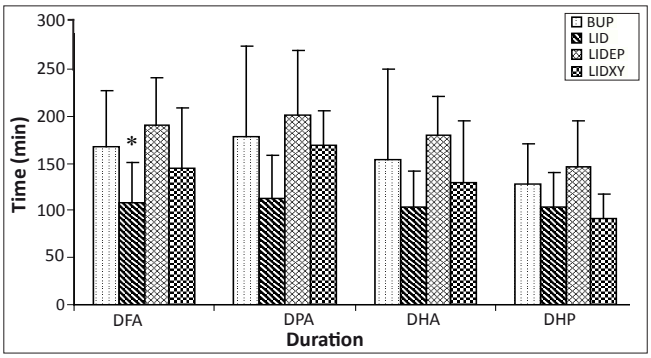
Lumbosacral epidural administration of anaesthetic agents is a classic technique used in small ruminants and swine for procedures including, (1) caesarean section, (2) laparotomy, (3) rumenotomy, (4) repair of rectal, uterine, or vaginal prolapse, (5) repair of abdominal, inguinal, or scrotal hernias and (6) surgery of the prepuce, penis, or hindlimbs.[2] The advantages of epidural anaesthesia as compared with line or inverted L infiltration anaesthesia include the use of a single injection of a small quantity of anaesthetic, lower potential risk of systemic local anaesthetic toxicity, and uniform analgesia and relaxation of the skin, musculature and parietal peritoneum.

Local anaesthetics have been combined with alpha$_2$-adrenergic agonist drugs in epidural or subarachnoid applications to obtain a long-lasting analgesia in sheep[18], goats[11,12,19] or calves[9,20]. Epidural lidocaine or xylazine has been used in combination with total intravenous anaesthesia in fat-tailed sheep undergoing hindlimb orthopaedic surgery.[21] Epidural xylazine produces profound analgesia by activation of alpha$_2$-receptors in the substantia gelatinosa

TABLE 1: Mean ± s.d. body weight, distance to epidural space, onset time (min) for flank (OFA), perineum (OPA) and hindlimb (OHA) analgesia and onset time for hindlimb paralysis (OHP) in sheep (n = 6) receiving epidural, lidocaine, lidocaine-epinephrine, lidocaine-xylazine or bupivacaine solutions.

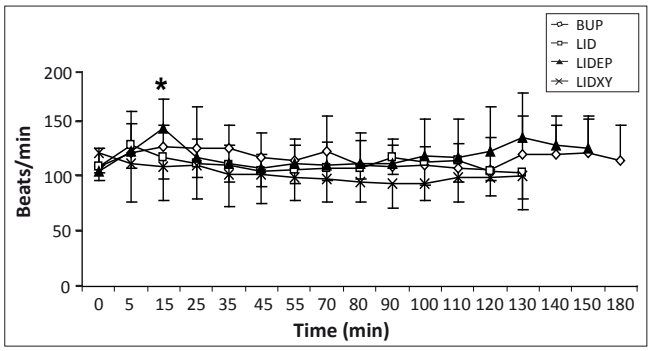
Treatments	LID	LIDEP	LIDXY	BUP
Body weight (kg)	22.4 ± 2.7	23.9 ± 2.5	25.4 ± 2.3	25.5 ± 2.8
Onset time of flank anaesthesia (min)	8.7 ± 6.8	5.3 ± 2.6	3.5 ± 2.6	7.0 ± 7.0
Onset time of perineum anaesthesia (min)	6.0 ± 4.0	8.7 ± 8.4	3.2 ± 1.9	7.8 ± 6.6
Onset time of hindlimb anaesthesia (min)	5.2 ± 4.3†	8.7 ± 4.5	3.5 ± 2.1‡	10.5 ± 5.0
Mean onset time of flank, perineum and hindlimb anaesthesia (min)	6.6 ± 5.1	7.6 ± 5.6	3.4 ± 2.1†	8.4 ± 6.1
Onset time of hindlimb paralysis (min)	5.0 ± 4.4	7.8 ± 5.2	3.5 ± 2.1‡	10.5 ± 5.0

LID, lidocaine; LIDEP, lidocaine-epinephrine; LIDXY, lidocaine-xylazine; BUP, bupivacaine.
†, Significant differences from the BUP group ($p < 0.05$).
‡, Significant differences from the LIDEP and BUP groups ($p < 0.05$).



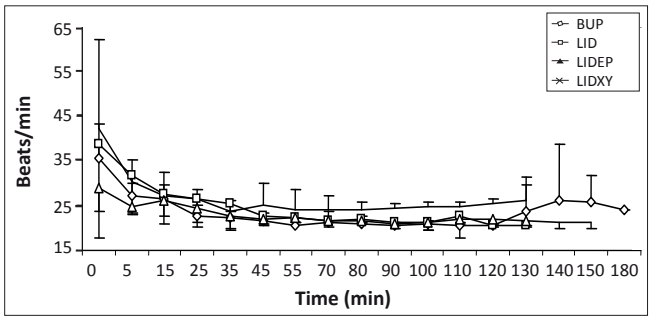
DFA, duration of flank analgesia; DPA, duration of perineum analgesia; DHA, duration of hindlimb analgesia; DHP, duration of hindlimb paralysis; BUP, bupivacaine; LID, lidocaine; LIDEP, lidocaine-epinephrine; LIDXY, lidocaine-xylazine.
*, Significant differences from LIDEP and BUP groups ($p < 0.05$).

FIGURE 1: Duration of complete anaesthesia (mean ± s.d.) at the flank, perineum and hindlimb and duration of hindlimb paralysis after epidural administration of lidocaine, lidocaine-epinephrine, lidocaine-xylazine or bupivacaine in fat-tailed sheep (n = 6).



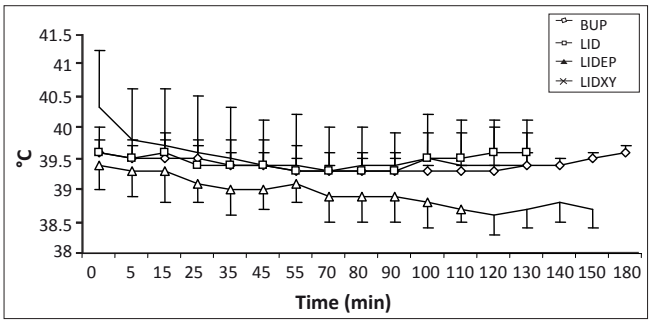
BUP, bupivacaine; LID, lidocaine; LIDEP, lidocaine-epinephrine; LIDXY, lidocaine-xylazine.
*, Significant difference from baseline in LIDEP group ($p \leq 0.05$).

FIGURE 2: Heart rate (mean ± s.d.) in sheep (n = 6) administered with epidural lidocaine, lidocaine-epinephrine, lidocaine-xylazine or bupivacaine.



BUP, bupivacaine; LID, lidocaine; LIDEP, lidocaine-epinephrine; LIDXY, lidocaine-xylazine.

FIGURE 3: Respiratory rate (mean ± s.d.) in sheep (n = 6) administered with epidural lidocaine, lidocaine-epinephrine, lidocaine-xylazine or bupivacaine.



BUP, bupivacaine; LID, lidocaine; LIDEP, lidocaine-epinephrine; LIDXY, lidocaine-xylazine.

FIGURE 4: Rectal temperature (mean ± s.d.) in sheep (n = 6) administered with epidural lidocaine, lidocaine-epinephrine, lidocaine-xylazine or bupivacaine.

of the dorsal horn of the spinal cord and inhibits the release of norepinephrine and substance P.[22] However, comparable analgesia of the perineum and flank has been observed in cattle following epidural or intramuscular administration of detomidine, a more selective alpha$_2$-agonist, suggesting the contribution of supraspinal analgesia following systemic drug absorption.[23]

In epidural anaesthesia, the extent of the anaesthetised area depends on the total dose (volume × concentration) of the anaesthetic administered. The volume of drug(s) used in the present study approximated 0.21 mL/kg (range, 0.19 mL/kg – 0.24 mL/kg). The recommended volume of lidocaine for anterior epidural anaesthesia in sheep and goats is about 0.20 mL/kg – 0.22 mL/kg (1.0 mL per 4.5 kg – 5.0 kg of body weight).[2] With this volume, anaesthesia can be expected to extend up to the umbilicus; however, repair of umbilical hernias may require the injection of a higher volume of local anaesthetic because the cranial aspect of the umbilicus is innervated by the 9th to 13th thoracic nerves.[13,20] Higher volumes of anaesthetic solutions injected into the epidural space produce a higher cranial migration of analgesics and improve the cranial spread of sensory blockade.[24] There is a tendency for a greater cranial spread of local anaesthetic solution within the epidural space in pregnant (owing to engorgement of epidural veins), obese (because of increased deposits of fat in epidural space) and geriatric (due to occlusion of intervertebral foramina and decreasing leakage of local anaesthetic solution) patients.[2] In the present study, the total volume injected epidurally was 5.0 mL in all sheep, regardless of body weight; therefore, the doses of lidocaine in the LID, LIDEP and LIDXY groups were 4.5 mg/kg, 4.2 mg/kg and 3.9 mg/kg, respectively. Sheep in the BUP group received 1.0 mg/kg bupivacaine. These doses are considerably lower than the toxic doses of lidocaine and bupivacaine in sheep.[25,26] Studies of the pharmacokinetics of lidocaine and bupivacaine and the effects of epinephrine or xylazine addition on the plasma concentration of local anaesthetics in sheep could provide useful information on systemic toxicity following epidural administration of local anaesthetics.

Gravity may also affect the spread of local anaesthetic solution within the epidural space in a patient in lateral recumbency or in a head-up or head-down position.[2] In the current study, sheep were maintained in the standing position following epidural injection and throughout the study period to promote bilateral anaesthesia.

Behavioural responses to painful stimuli are difficult to assess in sheep because of the animals' stoic nature. The use of a simple pain scoring system was chosen because, in most cases, muscle twitch was the only reliable response observed during noxious stimulation of the perineum and flank regions.

Lidocaine, the most commonly used local anaesthetic in clinical practice, has a rapid onset and moderate duration (60 min – 120 min) of action. The addition of epinephrine to lidocaine may slow the onset of action by decreasing the pH of anaesthetic solution and reducing the amount of non-ionised local anaesthetic.[3] In the present study, the addition of epinephrine (5 µg/mL) to lidocaine only changed the pH from 6.28 to 6.27 and, although the onset of sensory blockade in the hindlimb was significantly faster with LID than LIDEP (5.2 min vs 8.7 min), there was no significant difference, with respect to the mean onset of sensory blockade in the perineum, flank and hindlimb, between plain lidocaine and lidocaine containing epinephrine (6.6 min vs 7.6 min). It should be mentioned that the pH of freshly prepared lidocaine-epinephrine solution was higher than the pH of commercially available preparations containing epinephrine (6.27 vs 4.24). Although the onset of anaesthesia following epidural bupivacaine tended to be longer (mean 8.4 min),

this would not delay the start of any surgery. The longer onset of action for bupivacaine is attributed to its higher acid dissociation constant (pKa = 8.1) which decreases the percentage of the uncharged, non-ionised base form of local anaesthetic molecules.[3]

A delayed onset of analgesia following the epidural administration of xylazine has been reported in goats (mean onset of analgesia, 9.0 min – 9.5 min), buffalo calves (15.0 min), sheep (10.0 min) and cows (17.5 min).[10,12,27,28,29] The time required for the drug to reach its site of action in the spinal cord may account for the slow onset of action for xylazine.[22] The combination of LIDXY shortened the time to the onset of action because of the rapid onset of action for lidocaine.[30] The results of this study suggested that by mixing lidocaine and xylazine, the onset of sensory blockade may be faster when compared with LIDEP and BUP.

Epidural administration of LIDEP, LIDXY and BUP induced comparable anaesthesia of the flank, perineum and hindlimb. Although the duration of anaesthesia was not significantly different between LIDEP and the LIDXY groups, sheep in the LIDEP group tended to have a longer duration of action compared with the LIDXY group. A similar duration of action has been reported following subarachnoid administration of LID and LIDXY in goats.

The duration of action for a local anaesthetic is proportional to the time that the drug remains bound to the sodium channels. The addition of epinephrine to a local anaesthetic agent produces vasoconstriction at the injection site, which, in turn, reduces the rate of systemic absorption and prolongs the duration of the local anaesthetic effect.[3] It is interesting to note that epidural epinephrine, per se, has an antinociceptive effect, which is probably mediated by the activation of alpha$_2$-adrenoreceptors in the substantia gelatinosa of the spinal cord.[31] Epinephrine is effective when added to an anaesthetic solution in a concentration of 5 µg/mL – 20 µg/mL.[3] However, the optimal concentration of epinephrine for epidural anaesthesia is not known. The lowest recommended concentration of epinephrine (5 µg/mL) was used in the present study.

It has been shown that local anaesthetic combined with alpha$_2$-agonist drugs increases the duration of anaesthesia following epidural or subarachnoid administration.[15,18] The lack of significant difference in the duration of anaesthesia between LID and LIDXY groups in the present study may have been attributed to the small sample size of each group or low concentration of xylazine (0.05 mg/kg) added to lidocaine in this study. Following the epidural administration of LIDEP or BUP, anaesthesia can be expected to persist for up to 5 h, which provides an extended duration of surgical anaesthesia and pain management in the early postoperative period. Sheep in the LIDXY group received a full dose of lidocaine (5 mL, 2%) plus 0.05 mg/kg xylazine because it was of interest to compare the effects of the addition of xylazine or epinephrine to the lidocaine solution.

The duration of hindlimb paralysis was significantly shorter in the LIDXY group compared with the LIDEP group. Therefore, an epidural LIDXY block may offer advantages over LIDEP in patients undergoing caesarean section because recovery of motor function in the hindlimbs occurs faster, meaning that the dam would be able to stand and nurse the newborn soon after delivery. Immobility of the hindlimbs and relaxation of abdominal muscles is desirable during surgery because it facilitates restraint and positioning of the animal and prevents abdominal pressure, especially during surgical repair of abdominal hernias in sheep and goats.

A transient increase in HR was observed in sheep given epidural LIDEP, suggesting rapid systemic absorption of epinephrine from the epidural space following drug administration. The highly lipophilic nature of epinephrine allowed for rapid distribution of the drug out of the epidural space by way of the epidural vasculature.[32] Bradycardia and respiratory depression are common side effects following xylazine administration in ruminants. The change in HR, RR and SaO_2 levels was not significant in the LIDXY treatment; however, sheep in the LIDXY group had a lower HR compared with other groups. Similar results were obtained in sheep that received a subarachnoid combination of lidocaine and clonidine.[18] However, a significant decrease in HR and RR has been reported after subarachnoid administration of LIDXY in goats.[11] The possible reasons for this discrepancy are species differences (higher sensitivity of goats to xylazine) and/or the different route of drug administration (subarachnoid vs epidural).

Sedation and increased urination frequency are commonly observed following epidural administration of xylazine,[11] indicating rapid systemic absorption of xylazine from the epidural space. The mechanism of increased urination frequency after epidural LIDXY administration may be associated with the inhibition of an antidiuretic hormone released from the pituitary gland and the osmotic diuretic effect of hyperglycemia induced by xylazine.[33]

Neurotoxicity is one of the most serious adverse effects of neuraxial administration of drugs. It has been speculated that the vasoconstrictive effects of alpha$_2$-adrenergic agonists may reduce spinal blood flow, producing spinal ischaemia with neuronal damage. Lumbar epidural clonidine, an alpha$_2$-adrenergic agonist structurally related to xylazine, did not affect regional blood flow to the spinal cord in sheep.[34] Although no histologic damage has been observed after epidural administration of xylazine in horses[22,35] or clonidine in sheep[36], epidural administration of xylazine has recently been incriminated in irreversible paralysis of three cows and near fatal apnoea in one calf.[37] Although marked demyelinisation of the lumbar spinal cord was observed on necropsy, it is not clear whether the preservative or the drug itself is responsible for this reaction.

When appropriate doses are used, lumbosacral epidural anaesthesia with local anaesthetics produces minimal

haemodynamic and respiratory changes in conscious animals,[2] whilst epidural administration of alpha$_2$-agonists alone, or in combination with local anaesthetics, has been associated with hypotension, bradycardia, respiratory acidosis, hypoxemia, ruminal hypomotility, salivation and increased urine production.[10,19,29,38] Whilst these side effects are generally well-tolerated by young, healthy animals, significant morbidity and mortality may occur in patients having poor cardiopulmonary functions.[29]

The use of the LIDXY combination apparently offers no clinical advantages over LIDEP for the following reasons. Firstly, xylazine-induced cardiopulmonary depression may be detrimental in poor-risk patients.[29] The cardiopulmonary compromises may become more critical if the animal is placed in dorsal recumbency during surgery.[39,40] Secondly, systemic administration of alpha$_2$-adrenergic antagonists may not completely reverse xylazine-induced cardiopulmonary depression and sedation.[38] Thirdly, there is still uncertainty regarding neurotoxicity of xylazine or its preservative following neuraxial administration.[37] Fourthly, if concomitant (simultaneous) sedation is necessary, it is best to consider using small doses of intramuscular or intravenous xylazine or other sedative drugs. With systemic administration, the dose of xylazine could be adjusted to the animal's condition and the surgical procedure. In addition, xylazine could be administered in advance to facilitate epidural drug injection in excited, stressed animals.

Conclusion

Lumbosacral epidural LIDEP, LIDXY and BUP provide prolonged anaesthesia that may contribute to pain relief in the immediate postoperative period in animals undergoing surgical procedures involving the flank, perineum and hindlimb. The clinical use of epidural LIDXY can be indicated when a concomitant mild sedation is desired. Further studies are required to establish the optimum concentration of epinephrine or xylazine added to local anaesthetic solution for epidural anaesthesia in sheep.

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Competing interests

The authors declare that they have no financial or personal relationship(s) which may have inappropriately influenced them in writing this paper.

Authors' contributions

The authors made equal contributions to experimental project design and acquisition of data. N.V. (Shiraz University) was responsible for analysis of data and drafting the article.

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