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Comparison of Xylazine, Lidocaine, Xylazine-Lidocaine Lumbosacral Epidural on Analgesia and Cardiopulmonary Functions in Sedated West African Dwarf Goats

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ABSTRACT

Ruminants are commonly subjected to loco-regional anesthetic techniques over general anesthesia due to minimal side effects. There is still limited information on the effects of some drug protocols in use. This study investigated the analgesic and cardiopulmonary effects of some drugs for lumbosacral epidural in sedated goats. Six adult West African Dwarf bucks, mean body weight of 8.5 ± 2 kg were randomly selected for three separate crossover trials. Sedation was achieved with midazolam (0.03 mg/kg, IM) for all trials. Goats were given epidural injection of 2% lidocaine at 4.4 mg/kg (LGE), 2% xylazine at 0.15 mg/kg (XYE) and the mixture of 2% lidocaine (2.2 mg/kg) and 2% xylazine at 0.08 mg/kg (LXE) respectively. Venous blood was collected at 0, 30, 60, 90, and 180 minutes, to determine hematology changes. Heart rate, respiratory rate, and rectal temperature were recorded before epidural injection of the drugs in 10 minute intervals over a period of 180 minutes. Anesthetic indices were calculated and recorded. All data were analyzed using descriptive statistics and ANOVA at $p < 0.05$. Results showed that lidocaine treatment produced a significantly rapid (2.50 ± 1.98) onset of blockade earlier than xylazine/lidocaine (2.76 ± 1.03) and xylazine (3.50 ± 2.17), respectively. Xylazine/lidocaine combination produced a longer duration of analgesia (97.00 ± 12.17) than Lidocaine (26.7 ± 0.52) or xylazine alone (91.50 ± 10.84). Xylazine treatment produced a significantly longer duration (127.33 ± 22.02) of recumbency than lidocaine (22.32 ± 34.86) and xylazine/lidocaine (105.00 ± 33.95) mixture. All treatments showed no significant changes in hematological and biochemical parameters to warrant systemic dysfunction. The heart rate and rectal temperature were significantly lower with xylazine treatment compared with LGE and LXE groups. In conclusion, epidural injection of LXE produced a longer duration of analgesia, the optimum duration of recumbency, with a lesser dosage of both drugs and the least side effects.

Introduction

Goats are generally one of principal sources of meat and milk and the most countless among livestock reared in Nigeria.[1] They are mostly found in drier areas of the developing world and are able to reproduce throughout the year.[2] Goats play an important role in the socio-economic life of many rural communities of the world by contributing to food security and income to local farmers.[3] The West African Dwarf (WAD) goat is the most important and commonest indigenous breed of

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goats found in this region.[4,5] They have the ability to live under the most diverse conditions of natural habitat. This adaptability is due to certain definite physiological characteristics, which make them a very valuable asset for subsistence farmers. Besides, they have the ability to acclimatize, convert their feed into highly nutritious milk and meat very efficiently.[6,7] Due to the peculiarity of the digestive system, ruminants are not generally considered for general anesthesia.[8] Also, there is possibility of aspiration of ruminal content if the airway is left unprotected.[8-10] Complications such as ruminal tympany, marked cardiopulmonary depression, ptyalism are other main complications of general anesthesia in the digestive system of small ruminants.[8,10] Consequently, regional anesthesia produced by perineal or epidural injections of anesthetic agent is most frequently employed in ruminants.[11,12] Epidural anesthesia is a type of regional anesthesia that is commonly used in veterinary medicine to cause a reversible motor and sensory paralysis of the spinal nerve in domestic ruminants for diagnostic and surgical interventions at the perineal region, lower abdomen, flank, and in the tail.[13] Lumbosacral epidural anesthesia is simple, inexpensive, easy to administered and there no need for sophisticated equipment. It is commonly used in ruminants for obstetric procedures, caudal surgical procedures, and as an adjunct treatment for control of rectal tenesmus.[13-15] It is considered to be an effective method for providing anesthesia and postoperative analgesia.[8] Although there are several local anesthetics available for epidural analgesia, the most commonly used substance is lidocaine.[16] Lidocaine is considered to be a prototype of aminoamide family of drugs.[8,17] It is commonly used for local anesthesia of peripheral nerve, neuroaxial blockade, local infiltration, and for topical desensitization of mucosa or skin.[18] Studies have shown that lidocaine is widely used in all species because of its excellent diffusing and penetrating properties, and quick onset and intermediate duration of action.[19,20] However, lidocaine has a short half-life and therefore, cannot provide enough postoperative analgesia in major surgical procedures.[21-23] It is necessary to combine it with other drugs in order to increase the duration of nerve block in epidural analgesia.[24] Ideally, an epidural anesthetic agent should provide a long duration of analgesia, rapid onset of action and adequate muscle relaxation.[25] A major setback to lidocaine administration is larger volumes of the analgesic agent will be needed, which possess a high risk of motor paralysis to the hind limb. Alpha$_2$-adrenergic agonists and opioids have analgesic potential needed for surgical procedures that require long duration of analgesia. These agents selectively block sensory fibres, providing enough analgesia that will eliminate the possibility of any hind limb injuries.[26] Xylazine hydrochloride is the most commonly used sedative agent in ruminants.[8] Although, among all domestic animals, ruminants are believed to be the most sensitive to alpha-2 agonists.[27] Studies have shown that xylazine is associated with moderate to severe cardiopulmonary depression such as bradycardia, hypotension, tachypenia and hypoxemia.[28] A combination of xylazine and lidocaine into the epidural space has been shown to achieve faster onset of action and provides longer duration of analgesia.[29,30] Xylazine has been used in combination with propofol in sheep[31] and with ketamine in goats.[32] The ideal epidural anesthetic for goat should have combine the properties of rapid onset of action, optimal duration of action, long duration of analgesia, muscle relaxation, fast recovery and minimum side effects. A single drug cannot achieve these ideal and desirable properties and there is paucity of information on effects xylazine, lidocaine or xylazine-lidocaine mixture protocols for lumbosacral epidural in WAD goats. Therefore, this study was designed to investigate the analgesic and cardiopulmonary effects of xylazine, lidocaine and xylazine-lidocaine mixture for lumbosacral anesthesia in sedated WAD goats.

Materials and Methods

Ethical approval was obtained from the Animal Care and Use Research Ethics Committee (UI-ACUREC/054-0623/22) before the commencement of this study. Six WAD goats aged between 1 and 1.5 years and mean body weight of 8.5 ± 2 kg were used for the study. They were fed a basal diet of forage (*Cynodon alaferensis*), dry cassava peels and cereal-based concentrate. Fresh clean water was provided *ad libitum* in the pen, animals were judged to be in good health condition before the commencement of the experiment based on laboratory findings from normal hemogram and complete physical examination. The study design used was crossover trial where three experimental trials were carried out on the same group of animals, with 14 days period in between each trial for total wash out period of the drugs.[33,34] Sedation was achieved with intramuscular injection of midazolam (Verve Human Care Laboratories, 15A, Pharmacity, Selaqui, Uttarakhand, India) at 0.03 mg/kg for all the experimental trials. Before epidural injection, the lumbo-sacral area was aseptically prepared with povidone iodine (Apacco Pharmaceutical Ltd., Nigeria). Local infiltration (skin bleb) of 0.5 ml 2% Lidocaine (Swiss Parenterals Ltd., Gujarat, India) was performed around the site of injection to achieve a relatively painless epidural injection. For each experiment, goats were given epidural injection of 2% lidocaine at 4.4 mg/kg (LGE), 2% xylazine (Bioveta, a.s. Komenského, Czech Republic) at 0.15 mg/kg (XYE) and mixture of 2% lidocaine (2.2 mg/kg) and 2% xylazine at 0.08 mg/kg (LXE) respectively. The goat was placed on sternal recumbency

to palpate the injection site and perform epidural injection. Sterile 21-gauge hypodermic needle 0.8 mm × 40 mm (Uch-Jet Crystal-Uch Ltd., Nigeria) was inserted into the epidural space at the interspace between the last lumbar and the first sacral vertebrae after penetrating the *ligamentum flavum*. The correct positioning of the needle was confirmed by the absence of cerebrospinal fluid or blood at the hub and by absence of resistance while administering the appropriate anesthetic solution. The syringe containing the calculated volume of drug solution was attached to the inserted needle and solution injected. In all the animals, the drugs were administered epidurally through the lumbo-sacral interspace previously described,[35] with the injection taking over 20 seconds. The development of neural blockade was judged once the animals were unable to stand on their hind limbs. Thereafter, they were placed on right lateral recumbency. Serial pinching of the skin of the goats' hind limbs and interdigital space of the hind limbs with a hemostatic forceps close to the first ratchet, as described in previous similar studies,[36] was used to determine the onset, extent and duration of analgesia on all or none basis. Venous blood via jugular venepuncture was collected at 0 minute, 30 minutes, 60 minutes, 90 minutes and 180 minutes, to determine hematology and biochemical changes. Heart rate (beats/minute), respiratory rate (breath/minute), and rectal temperature (°C) were recorded before epidural injection of the drugs at 0 minute and at 10 minute interval over a period of 180 minutes. Anesthetic indices were calculated and recorded for all the experimental trials; time of recumbency (in minutes) was defined as time interval between epidural injections of anesthetic solution to paralysis of the goats' hind limbs. Time of onset of analgesia was calculated (in minutes) from the time of epidural injection of anesthetic solution to loss of reflex response to pinching with artery forceps. Duration of analgesia (in munities) was determined by the return to pedal reflex response with artery forceps. Duration of recumbency (in minutes) was recorded from the time of the blockade to the goats' ability to stand). Data were expressed as mean ± SD and were analysed using multiple t-test and statistical significance determined using the Holm-Sidak method. Value of < 0.05 were considered significant. GraphPad Prism, version 8.02 for windows (GrapPad Software, San Diego, CA, USA) was used for the analysis.

Results

The xylazine/lidocaine mixture (LXE) group had a significantly longer time of induction (27.67 ± 14.4 minutes) compared to the xylazine alone (XYE) group (22.17 ± 3.60 minutes). The onset of blockade was similar across all three groups, ranging from 2.50 ± 1.98 minutes (LGE) to 3.50 ± 2.17 minutes (XYE). The LXE group had a significantly longer duration of analgesia (97.00 ± 12.17 minutes) compared to the LGE group (26.7 ± 0.52 minutes). The XYE group had a significantly longer duration of recumbency (127.33 ± 22.02 minutes) compared to the LGE group (22.32 ± 34.86 minutes) (Table 1). The packed cell volume was significantly lower in the XYE group compared to the LGE group at 30- and 60-minutes post-injection. The hemoglobin concentration followed a similar trend, with the XYE group having significantly lower values compared to the LGE group at 30 and 60 minutes. The red blood cell count was significantly lower in the XYE group compared to the LGE group at 30 minutes. There were no significant differences in white blood cell count, platelet count, or differential leukocyte counts among the groups (Table 2). There were no significant differences in total protein, albumin, globulin, albumin/globulin ratio, urea/nitrogen ratio, creatinine, AST, or alkaline phosphatase among the groups at any time point. The XYE group had significantly lower ALT values compared to the LXE group at all time points. The LGE group had significantly higher blood glucose levels compared to the XYE and LXE groups at all-time points (Table 3).

Figure 1 depicts the changes in heart rate over time in response to epidural administration of three different treatments: xylazine alone (XYE), lidocaine alone (LGE), and a combination of xylazine and lidocaine (LXE). The x-axis represents the time points at which heart rate measurements were taken, ranging from 0 minutes (baseline) to 180 minutes post-injection. The y-axis represents the heart rate values in beats per minute (bpm). At baseline (0 minutes), the heart rates were similar across all three treatment groups. After epidural injection, the LGE group (lidocaine alone) showed a significant increase in heart rate compared to the XYE group (xylazine alone), as indicated by the superscripts "a" and "b" at various time points. The LXE group (xylazine-lidocaine mixture) also exhibited a significant increase in heart rate compared to the XYE group, as denoted by the superscripts c and d at several time points. However, there were no significant differences in heart rate between the LGE and LXE groups.

Table 1. The Anesthetic indices of 6 sedated WAD goats following epidural injection

Parameters	XYE	LGE	LXE
Time of induction after sedation	22.17 ± 3.60[a]	23.33 ± 8.16	27.67 ± 14.4[b]
Onset of blockade	3.50 ± 2.17	2.50 ± 1.98	2.76 ± 1.03
Duration of analgesia	91.50 ± 10.84	26.7 ± 0.52[a]	97.00 ± 12.17[b]
Duration of recumbency	127.33 ± 22.02[b]	22.32 ± 34.86[a]	105.00 ± 33.95

Mean ± SD, n = 6. XYE: xylazine, LGE: lidocaine, LXE: xylazine/lidocaine. Values with superscripts [a,b] are significantly ($p < 0.05$) different

Table 2. Hematological responses of sedated WAD goats to epidural blockade with xylazine, lidocaine and xylazine-lidocaine mixture

Parameters	0 min			30 min			60 min			90 min			180 min			Ref value
	LGE	XYE	LXE	LGE	XYE	LXE	LGE	XYE	LXE	LGE	XYE	LXE	LGE	XYE	LXE	
Packed cell volume (%)	20.3 ± 2.3	21.3 ± 1.4	17.0 ± 1.8	21.7 ± 1.5[a]	17.0 ± 2.3[b]	15.0 ± 1.7[b]	20.3 ± 5.1[a]	18.2 ± 2.9	15.5 ± 1.6[b]	20.7 ± 2.3	18.2 ± 3.4	15.8 ± 2.7	20.7 ± 1.6	19.3 ± 3.2	17.5 ± 2.7	22-38
Hemoglobin concentration (g/dl)	6.5 ± 0.8	6.8 ± 0.5	5.4 ± 0.5	6.9 ± 0.6[a]	5.5 ± 0.8[b]	4.8 ± 0.5[b]	6.6 ± 1.7	5.6 ± 1.0	4.9 ± 0.5	6.6 ± 1.1	5.8 ± 1.1	4.9 ± 1.0	6.5 ± 0.5	6.2 ± 1.2	5.4 ± 1.0	8-12
Red Blood Cell (× 10^6/µl)	10.0 ± 2.1	10.6 ± 1.0	8.6 ± 0.8	10.8 ± 1.9[a]	8.8 ± 0.9	8.1 ± 0.5[b]	9.5 ± 1.8	9.5 ± 1.4	8.1 ± 0.6	10.1 ± 1.9	9.2 ± 1.8	8.2 ± 1.2	10.2 ± 1.8	9.8 ± 1.5	9.0 ± 1.4	8-18
White blood cell (× 10 × 10^3/µl)	6.2 ± 3.3	10.0 ± 6.8	8.2 ± 2.1	7.6 ± 0.9	10.0 ± 5.3	5.6 ± 2.2	8.0 ± 2.5	9.9 ± 6.6	6.5 ± 1.8	7.0 ± 3.1	9.1 ± 6.9	7.5 ± 3.4	8.5 ± 2.2	8.7 ± 5.5	5.4 ± 2.6	4-13
Platelet	143.1 ± 85.6	130.5 ± 36.1	139.3 ± 28.4	141.0 ± 65.6	106.3 ± 49.9	118.1 ± 43.8	140.8 ± 48.6	147.0 ± 61.1	143.0 ± 39.8	161.3 ± 46.3	129.8 ± 46.8	132.2 ± 16.9	154.3 ± 38.0	116.2 ± 38.2	377.5 ± 60.1	300-600
Lymphocytes (%)	45.0 ± 6.0	52.0 ± 13.4	53.8 ± 15.4	48.7 ± 8.2	54.3 ± 11.7	49.7 ± 12.2	42.7 ± 5.9	55.5 ± 13.2	48.0 ± 9.3	49.2 ± 3.2	56.3 ± 13.2	50.8 ± 13.2	42.5 ± 7.7	54.0 ± 13.8	54.2 ± 11.6	2000-9100
Neutrophils (%)	52.3 ± 7.3	42.5 ± 14.2	41.0 ± 16.9	48.5 ± 7.2	41.5 ± 12.4	45.8 ± 13.4	54.0 ± 5.5	40.3 ± 13.4	48.3 ± 7.6	48.7 ± 3.0	40.0 ± 13.3	45.7 ± 12.6	54.2 ± 7.9	41.3 ± 13.6	41.8 ± 12.3	1200-7200
Monocytes (%)	1.3 ± 1.0	2.5 ± 1.0	2.5 ± 1.4	1.8 ± 0.4	1.7 ± 0.8	2.3 ± 1.0	1.7 ± 0.5	2.0 ± 0.9	2.0 ± 1.4	0.8 ± 0.4	2.3 ± 1.0	1.7 ± 1.2	2.0 ± 0.9	2.0 ± 1.1	2.0 ± 0.9	0-550
Eosinophils (%)	1.7 ± 0.8	3.0 ± 1.7	2.3 ± 1.6	1.2 ± 1.2	2.5 ± 0.8	2.2 ± 1.0	1.7 ± 0.8	2.2 ± 1.0	1.8 ± 1.2	1.5 ± 0.5	3.0 ± 1.3	1.8 ± 1.3	1.3 ± 1.2	2.7 ± 0.8	2.0 ± 0.6	50-1050

Mean ± SD, n = 6. XYE: xylazine, LGE: lidocaine, LXE: xylazine/lidocaine. Values with superscripts [a,b] are significantly ($p < 0.05$) different.

Table 3. Biochemical changes in Sedated goats to epidural blockade with xylazine, lidocaine and xylazine-lidocaine mixture.

Parameters	0 min			30 min			60 min			90 min			180 min			Ref value
	LGE	XYE	LXE	LGE	XYE	LXE	LGE	XYE	LXE	LGE	XYE	LXE	LGE	XYE	LXE	
Total protein (g/dl)	6.6 ± 0.3	6.7 ± 0.5	6.9 ± 0.4	6.6 ± 0.2	6.6 ± 0.5	6.5 ± 0.3	6.6 ± 0.4	6.6 ± 0.5	6.5 ± 0.3	6.6 ± 0.4	6.6 ± 0.4	6.5 ± 0.2	6.6 ± 0.4	6.7 ± 0.3	6.7 ± 0.2	6-7.5
Albumin (g/dl)	2.7 ± 0.2	2.7 ± 0.2	3.0 ± 0.2	2.7 ± 0.2	2.7 ± 0.2	2.7 ± 0.2	2.6 ± 0.3	2.6 ± 3.0	2.6 ± 0.1	2.6 ± 0.2	2.8 ± 0.2	2.6 ± 0.2	2.6 ± 0.3	2.7 ± 0.1	2.8 ± 0.1	2-4.4
Globulin (g/dl)	4.0 ± 0.2	3.9 ± 0.3	4.0 ± 0.2	4.0 ± 0.1	3.9 ± 0.1	3.9 ± 0.1	4.0 ± 0.2	4.0 ± 0.3	3.9 ± 0.2	4.0 ± 0.2	3.9 ± 0.3	3.9 ± 0.1	4.0 ± 0.2	3.9 ± 0.3	3.9 ± 0.2	2.7-4.1
Albumin/Globulin ratio	0.67 ± 0.04	0.69 ± 0.07	0.74 ± 0.04	0.66 ± 0.05	0.68 ± 0.04	0.68 ± 0.06	0.65 ± 0.04	0.66 ± 0.10	0.66 ± 0.02	0.65 ± 0.03	0.71 ± 0.06	0.67 ± 0.05	0.66 ± 0.07	0.69 ± 0.05	0.72 ± 0.05	-
Urea/Nitrogen ratio (mg/dl)	12.5 ± 1.0	11.5 ± 1.7	14.4 ± 1.5	12.6 ± 0.7	11.4 ± 1.9	12.4 ± 1.1	11.7 ± 1.9	11.5 ± 2.1	12.7 ± 1.7	11.8 ± 1.5	11.7 ± 2.2	12.3 ± 1.0	11.9 ± 1.3	11.4 ± 1.3	13.6 ± 1.3	13-28
Creatinine (mg/dl)	1.0 ± 0.1	1.0 ± 0.1	1.2 ± 0.1	0.97 ± 0.1	1.02 ± 0.1	1.02 ± 0.1	0.95 ± 0.1	1.03 ± 0.2	0.98 ± 0.1	0.93 ± 0.1	1.0 ± 0.1	0.92 ± 0.0	0.93 ± 0.1	1.01 ± 0.1	1.05 ± 0.1	0.9-1.8
Aspartate aninotransferase (ul)	173.0 ± 6.0	175.0 ± 4.6	175.2 ± 6.6	175.3 ± 5.2	171.3 ± 7.5	170.2 ± 2.4	170.2 ± 8.2	174.0 ± 7.9	167.7 ± 4.7	171.2 ±10.1	172.7 ± 7.2	168.7 ± 3.9	172.8 ±10.4	174.0 ± 7.1	170.5 ± 5.0	60-280
Alanine aninotransferese (ul)	12.2 ± 1.8	7.3 ± 1.4	14.7 ± 1.5	12.3 ± 1.5	7.0 ± 1.5	13.7 ± 1.2	10.3 ± 2.3	7.2 ± 1.3	13.8 ± 1.3	10.8 ± 2.2	7.3 ± 1.0	13.3 ± 1.5	10.2 ± 1.5	7.7 ± 1.0	13.5 ± 1.4	-
Alkaline phosphatase (ul)	87.5 ± 7.5	97.5 ± 5.6	101.3 ± 3.2	87.7 ± 6.5	97.8 ± 7.5	97.0 ± 1.8	84.7 ±15.1	98.2 ± 7.1	96.2 ± 4.2	85.0 ±10.5	97.8 ± 8.1	97.7 ± 3.1	83.2 ± 8.6	100.7 ± 9.7	102.2 ± 5.4	9-131
Blood glucose (mg/dl)	87.0 ±13.7	55.7 ± 4.0	64.8 ± 4.5	89.2 ±11.4	55.0 ± 4.2	59.5 ± 5.5	81.2 ±13.9	53.5 ± 5.4	55.5 ± 6.7	80.7 ±12.6	56.2 ± 3.0	56.5 ± 5.1	82.8 ±12.4	53.2 ± 3.0	61.0 ± 4.6	50-80

Mean ± SD, n = 6. XYE: xylazine, LGE: lidocaine, LXE: xylazine/lidocaine.

Figure 2 illustrates the changes in rectal temperature over time in response to epidural administration of the same three treatments: xylazine alone (XYE), lidocaine alone (LGE), and a combination of xylazine and lidocaine (LXE). The x-axis represents the time points at which rectal temperature measurements were taken, ranging from 0 minutes (baseline) to 180 minutes post-injection. The y-axis represents the rectal temperature values in degrees Celsius (°C). At baseline (0 minutes), the rectal temperatures were similar across all three treatment groups. After epidural injection, the XYE group (xylazine alone) showed a significant decrease in rectal temperature compared to the LGE group (lidocaine alone), as indicated by the superscripts "a" and "b" at various time points. The LXE group (xylazine-lidocaine mixture) also exhibited a significant decrease in rectal temperature compared to the LGE group, as denoted by the superscripts e and f at several time points. Additionally, the LXE group had a significant decrease in rectal temperature compared to the XYE group, as

indicated by the superscripts c and d at certain time points.

Figure 3 illustrates the changes in respiratory rate over time in response to epidural administration of three different treatments: xylazine alone (XYE), lidocaine alone (LGE), and a combination of xylazine and lidocaine (LXE). The x-axis represents the time points at which respiratory rate measurements were taken, ranging from 0 minutes (baseline) to 180 minutes post-injection. The y-axis represents the respiratory rate values in breaths per minute (bpm). At baseline (0 minutes), the respiratory rates were similar across all three treatment groups. After epidural injection, the XYE group (xylazine alone) exhibited a significant decrease in respiratory rate compared to the LGE group (lidocaine alone) at most time points, as indicated by the lack of overlapping error bars. The LXE group (xylazine-lidocaine mixture) also showed a significant decrease in respiratory rate compared to the LGE group, as evident from the non-overlapping error bars. However, there were no clear significant differences in respiratory rate between the XYE and LXE groups, as their error bars overlapped at most time points.

Discussion

This work was designed to compare the analgesia and cardiopulmonary effects of xylazine, lidocaine and xylazine-lidocaine combination in midazolam sedated WAD goats. More specifically, this research clearly showed that xylazine-lidocaine administered into the epidural space could be useful clinically to provide rapid onset, prolonged and safe epidural analgesia which is required for long duration surgical and obstetrical

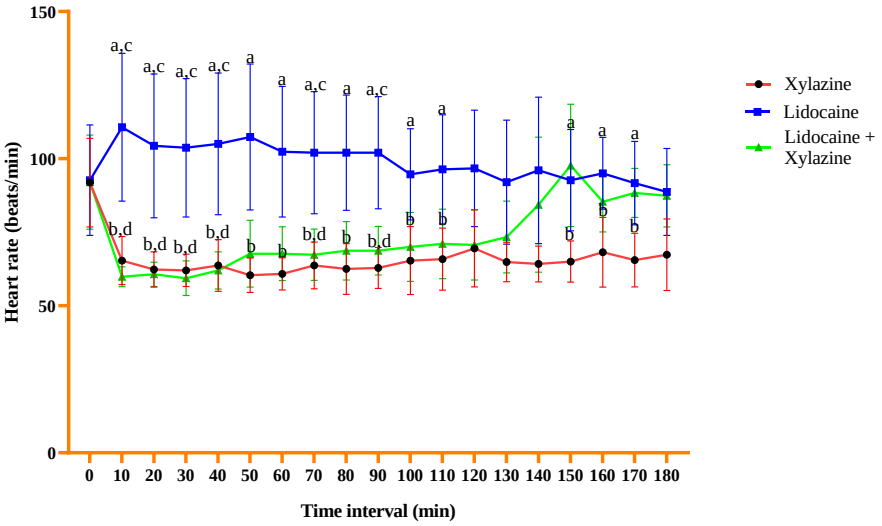

Figure 1. Comparison of heart rate response of six sedated goats during lumbo-sacral epidural block with xylazine, lidocaine and xylazine-lidocaine mixture. Letters [a,b] indicate significant ($p < 0.05$) difference between lidocaine and xylazine. Letters [c,d] indicate significant ($p < 0.05$) difference between xylazine alone and xylazine-lidocaine mixture.

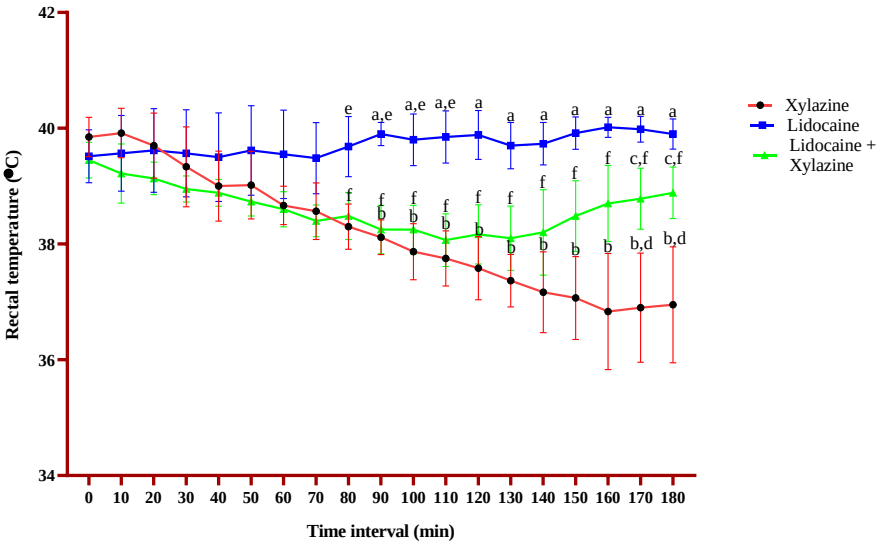

Figure 2. Comparison of rectal temperature response of six midazolam sedated goats during lumbo-sacral epidural block with xylazine, lidocaine and xylazine-lidocaine mixture. Letters [a,b] indicate significant ($p < 0.05$) difference between lidocaine and xylazine. Letters [c,d] indicate significant ($p < 0.05$) difference between xylazine-lidocaine mixture and xylazine alone. Letters [e,f] indicate significant ($p < 0.05$) difference between lidocaine alone and xylazine-lidocaine mixture.

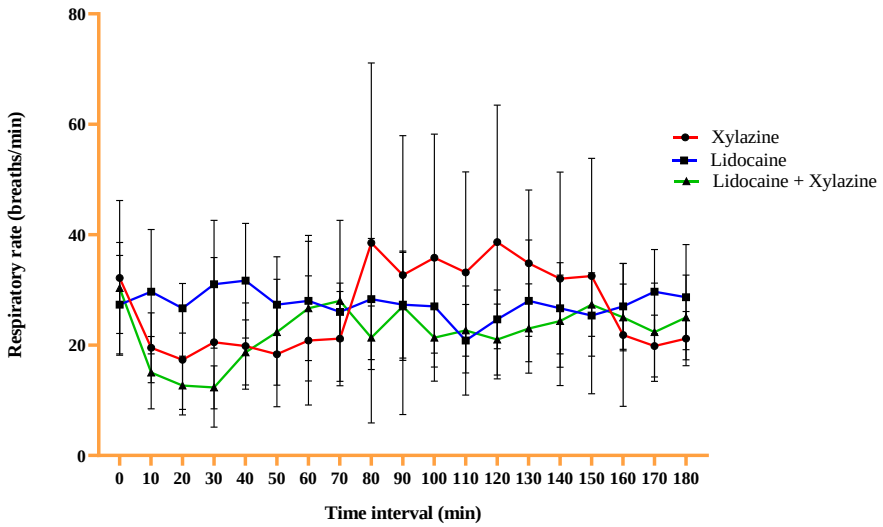

Figure 3. Comparison of respiratory rate response of six midazolam sedated goats during lumbo-sacral epidural block with xylazine, lidocaine and xylazine-lidocaine mixture.

operations in goats.[37-40] Conscious efforts were made in this study to exclude obese, pregnant, and geriatric goats as these factors are known to interfere with the movement of anesthetic agents within the epidural spacewhich is one of the reasons epidural nerve block was used as it is safe and effective technique that provide localized anesthesia and pain management with general anesthesia.[8,41-43]

The result of this study indicated that lumbosacral epidural administration of xylazine-lidocaine combination induced analgesia on the toe-web of the hind limb, tail and perineum in WAD goats, and the degree of analgesia was more profound, and duration was greater than that induced by the use of xylazine or lidocaine alone. This study also showed that xylazine-lidocaine combination had similar onset of analgesia with xylazine alone, but longer time of recumbency, longer duration of analgesia than lidocaine and xylazine alone. In the lidocaine treatment group, the analgesia produced by lumbosacral injection of lidocaine had a faster onset of analgesia than that produced by xylazine and xylazine-lidocaine. This corroborate with similar studies in goats and in cows using medetomidine.[44,45] A delayed onset of analgesia by xylazine compared to lidocaine has been reported in various animals.[46-49]

Midazolam was the sedative of choice for this study because it causes a mild cardio-respiratory effects and centrally-induced muscle relaxation.[50-52] Whereas, midazolam is administered in goats at a dose rate of 0.3-0.6 mg/kg IM to achieve hypnosis and light sedation.[53,54] The intravenous route was employed in this study but the lower dose rate of 0.03 mg/kg to reduce its effects on cardio-respiratory system.[55,56]

Recent research findings evaluated the analgesic effects of different anesthetic drugs and their combinations with variable results, similar study has been done in water Buffalo calves where it was concluded that there is a possible addictive analgesia interaction between epidurally administered xylazine and lidocaine, without causing any marked systemic effects in water buffalo calves.[57] In this study, the treatment designs were divided into 3 treatment protocols. Epidural injection of xylazine-lidocaine mixture produced a longer duration of analgesia but a shorter duration of recumbency. The long duration of analgesia of 97.00 ± 12.17 min in the xylazine-lidocaine group (LXE) is longer than the established duration of about 60 minutes by plain lidocaine.[8] This prolong analgesia is clearly attributable to xylazine in the mixture. Furthermore, this findings is consistent with a longer duration of analgesia with xylazine-lidocaine than lidocaine alone without any effects in previous studies.[38]

In this study, the animals showed signs of incoordination after the administration of lidocaine, this corroborated with a study conducted by Zayed *et al*. (2020) where lidocaine elicited incoordination in the hind limbs of goats.[58] Lidocaine is a commonly used local anesthetic drug in small ruminants to induce epidural anesthesia for a variety of obstetrical procedures which in most cases will require a large volume to cause ataxia or even recumbency.[13,59] Lidocaine works by inhibiting propagation and conduction of nerve impulses through the blockade of sodium channels in cells with subsequent prevention of depolarization.[60]

The results of this study showed that epidural xylazine-lidocaine induced analgesia in the skin of the hind limb, toes, perineum and the tail in goats, and the degree of analgesia was more profound and the duration was greater than that induced by the use of xylazine or lidocaine alone. Adverse effects of xylazine injected into the lumbosacral epidural space included increased salivation, decrease in heart rate and respiratory rate, sedation, recumbency, and ataxia In this study, xylazine-

lidocaine combination at a dosage of 0.08 mg/kg and 2.2 mg/kg respectively, administered via lumbosacral epidural injection produced analgesia with longer duration to that observed after the administration of xylazine or lidocaine alone. The onset of the analgesia of the studied region was more delayed in the xylazine treatment alone group XYL, while lidocaine treatment group had the fastest time of onset of analgesia. Analgesia produced by epidural or subarachnoid administration of lidocaine has a faster onset compared to xylazine in goats and medetomidine in cows.[44,61] Similar results were obtained in this study with xylazine producing a delayed response to the onset of analgesia. A delayed onset of analgesia by xylazine compared to lidocaine has been reported in various ruminates.[46-48] The duration of analgesia in the regions of the body that was studied after epidural administration of the half-doses of xylazine caused analgesia with a longer duration than that observed with the use of either drug alone at full dose. Analgesia produced by xylazine may be due to the inhibition of the release of substance p at the level of substantia gelatinosa of the dorsal horn of the spinal cord.[37] Xylazine may also have a local anesthetic-like effects on spinal nerves.[62]

Co-administration of alpha-2 agonist and local anesthetics provides prolonged analgesia in human, horses, llamas, dogs, cows and buffalos.[30] All the animals given the three treatment- xylazine, lidocaine and xylazine-lidocaine manifested in coordination and recumbency, with the xylazine-lidocaine group having more delayed recumbency which suggests that xylazine may also have had a local analgesic action, It has been suggested that some of the efficacy of alpha-2 adrenergic agonists in producing analgesia following their regional injection may result from their local anesthetic action on A and C fibres.[50,63] In the xylazine-lidocaine group of this experiment, the analgesic effect achieved was much more than in the other two groups. This could be attributed to different sites of action of both drugs. Situation of post-junctional alpha-2 adrenoceptors located to arterial and venous vasculature often produces vasoconstriction.[64]

The hematological values observed in this study were within the normal range for West African Dwarf goats.[65,66] In a study conducted,[8] lignocaine has been discovered to regulate cardiac arrhythmia and controlling automaticity, this is suggested to have helped to keep the hematological parameters within the normal range.

Side effects of epidurally administered xylazine and xylazine-lidocaine were manifested by profound sedation and salivation, similar to those reported after subarachnoid xylazine administration in goats or cattle,[27,67] indicating rapid vascular of lymphatic absorption from epidural space. All experimental goats showed an increase in the frequency of urination after epidural administration of xylazine and xylazine-lidocaine. This effect may be associated with the inhibition of antidiuretic hormone release from pituitary, antagonism of the renal tubular action of antidiuretic hormone, increase in glomerular filtration rate and release of atrial natriuretic factor.[68] The decrease in rectal temperature observed in the goats after the injection of xylazine into the epidural space has been attributed to the depression of the hypothalamic thermoregulatory centre causing sedation, reduced metabolism, muscle relaxation and depression of the CNS.[27,37] A decrease in rectal temperature after anesthetics injection has been reported in previous studies in goats.[27,48] In this study, lidocaine induced a long-lasting decrease in rectal temperature, possibly because of regional vasodilatation induced by the anesthetics. This findings corroborate with a study carried out by.[49]

In this study, administration of epidural xylazine in the goats of group XYE and LXE caused significant decreased in heart rate, respiratory rate and rectal temperature at different measurement points. Reduction in heart rate were reported after epidural injection in cattle, sheep, mares and goats.[67,69,70,27,48] A significant decrease in heart rate is considered a classical response following the injection of alpha-2 adrenoceptor agonist.[71] The bradycardia recorded after the administration of xylazine could be attributed to decreased sympathetic outflow from central nervous system inhibition of norepinephrine release from sympathetic nerve terminals, direct depression of cardiac pace maker and conduction tissue, increased vagal tone and a direct increase in the release of acetylcholine from parasympathetic nerves in the heart.[72]

According to the results of this study, the combination of xylazine with lidocaine (0.08 mg/kg and 2.2 mg/kg) produces comparable degrees of complete lumbosacral epidural analgesia to that of lidocaine or xylazine used alone. However, the combinations produced transient changes in the physiological parameters as a result of the sedative effects of the xylazine. The cardiopulmonary changes were transient and improved during the study as the effects of the drug wore off. The combinations may be used in clinical situations where longer duration of regional analgesia is required. Further research is needed to study the mechanism of interaction of lidocaine and xylazine at the spinal cord level in goats.

In conclusion, this study was able to establish that epidural injection of xylazine-lidocaine mixture (0.08 mg/kg and 2.2 mg/kg) produced a longer duration of analgesia which is highly desirable to handle post-operative pain. Also, less dosage of lidocaine and xylazine was sufficient to produce this desirable effect. Moreover, less side effects of both drugs was recorded as less dosage was administered. Also, the anesthetic protocols used in

this study did not affect the hematological parameters adversely as no significant changes to cause clinical emergency were observed. This could be ascribed to lesser dose administered with lidocaine-xylazine mixture, such protocol may be useful in clinically morbid goats. Moreover, no significant changes was observed in the biochemical parameters evaluated. This can be concluded that these three drug protocols used in this research are safe but the protocol involving the mixture of 0.08 mg/kg xylazine and 2.2 mg/kg lidocaine produced optimum duration of analgesia, recumbency, and least side effects.

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Conflict of Interest

Authors declare no conflict of interest.

References

1. Adeyinka IA, Mohammed ID. Relationship of liveweight and linear body measurement in two breeds of goat of Northern Nigeria. *Journal of Animal and Veterinary Advances.* 2006; 5(11): 891-893.
2. Omontese BO, Rekwot PI, Ate IU, Ayo JO, Kawu MU, Rwuaan JS, Nwannenna AI, Mustapha RA, Bello AA. An update on oestrus synchronisation of goats in Nigeria. *Asian Pacific Journal of Reproduction*. 2016; 5(2): 96-101. doi: 10.1016/j.apjr.2016.01.002
3. Kosgey IS. Breeding objectives and breeding strategies for small ruminants in the tropics. Ph.D. Thesis, Wageningen University, The Netherlands, 2004: 272.
4. Chiejina SN, Behnke JM, Fakae BB. Haemonchotolerance in West African Dwarf goats: contribution to sustainable, anthelmintics-free helminth control in traditionally managed Nigerian dwarf goats. *Parasite*. 2015; 22: 7. doi: 10.1051/parasite/2015006
5. Oseni NT, Fernando WM, Coorey R, Gold I, Jayasena V. Effect of extraction techniques on the quality of coconut oil. *African Journal of Food Science*. 2017; 11(3): 58–66. doi: 10.5897/AJFS2016.1493
6. Peacock C. Goats-A pathway out of poverty. *Small Ruminant Research*. 2005; 60: 179–186. doi: 10.1016/j.smallrumres.2005.06.011
7. Moses OD. Application of factor analysis scores in a multiple linear regression model for the prediction of liveweight in immature West African dwarf goat. *Philipp Journal of Veterinary Animal Science*. 2010; 36(2): 167-174.
8. Clarke KW, Trim CM, Hall LW: Anesthesia of sheep, goats, and other herbivores. In: Clarke KW, Trim CM, Hall LW: editors. *Veterinary Anesthesia*. 11th edn, Edinburgh; Saunders/Elsevier: 2014: 345–383.
9. Devendra C. The digestive efficiency of goats. *World Review of Animal Production*. 1978; 14(1): 9-22.
10. Eze CA, Idowu OS. Distribution of surgical cases at the university of Nigeria veterinary teaching hospital (1985—1995). *Tropical Veterinarian*. 2002; 20 (1): 52-56.
11. Taylor PM. Anesthesia in sheep and goats. *In Practice*. 1991; 13(1): 31-36. doi: 10.1136/inpract.13.1.31
12. Sadegh AB, Shafiei Z, Nazhvani SD. Comparison of epidural anesthesia with lidocaine-distilled water and lidocaine-magnesium sulfate mixture in goat, *Veterinarski Arhiv*. 2009; 79(1): 11–17.
13. Khajuria A, Shah RA, Bhat MH, Khan FA, Yaqoob SH, Naykoo NA, Ganai NA. Comparison between lignocaine hydrochloride and ropivacaine hydrochloride as lumbosacral epidural anesthetic agents in goats undergoing laparoscopy assisted embryo transfer. *Macedonian Veterinary Review*. 2014; 37(2): 141-149.
14. Lee I, Yoshiuchi T, Yamagishi N, Oboshi K, Ayukawa Y, Sasaki N, Yamada H. Analgesic effect of caudal epidural ketamine in cattle. *Journal of Veterinary Science*. 2003; 4(3): 261-264. doi: 10.4142/jvs.2003.4.3.261
15. Skarda RT, Tranquilli WJ. Local and regional anesthetic and analgesic techniques: ruminants and swine. *Lumb & Jones' veterinary anesthesia and analgesia*. 2007: 643-681.
16. Adetunji A, Ajadi RA, Aladesawe TA. A comparison of epidural anesthesia with lignocaine, bupivacaine and lignocaine/bupivacaine mixture in dogs. *Israel Journal of Veterinary Medicine*. 2001; 56(3): 85-89.
17. Steagall PV, Simon BT, Teixeira Neto FJ, Luna SP. An update on drugs used for lumbosacral epidural anesthesia and analgesia in dogs. *Frontiers in Veterinary Science*. 2017; 4: 68. doi: 10.3389/fvets.2017.00068
18. Pereira FG, Greene SA, McEwen MM, Keegan R. Analgesia and anesthesia in camelids. *Small Ruminant Research*. 2006; 61(2-3): 227-233. doi: 10.1016/j.smallrumres.2005.07.013
19. Dunlop CI, Hoyt Jr RF. Anesthesia and analgesia in ruminants. *Anesthesia and Analgesia in Laboratory Animals*. 1997: 281-311. doi: 10.1016/B978-012417570-9/50016-7
20. Magnusson BM, Walters KA, Roberts MS. Veterinary drug delivery: potential for skin penetration enhancement. *Advanced Drug Delivery Reviews*. 2001; 50 (3): 205-227. doi: 10.1016/S0169-409X(01)00158-2
21. Tiwari SK, Kumar A. Clinico-physiological effects of epidural xylazine and detomidine with or without local anesthetics in buffaloes (Bubalus bubalis). *Indian Journal of Veterinary Surgery*. 1998; 19(1): 37-38.
22. Singh P, Pratap K, Kinjavdekar P, Aithal HP, Singh GR. Effects of xylazine, lignocaine and their combination for lumbar epidural analgesia in water buffalo calves (*Bubalus bubalis*). *Journal of the South African Veterinary Association*. 2005; 76(3): 151-58. doi: 10.4102/jsava.v76i3.417
23. Adetunji A, Ajadi RA, Opia RE. A comparison of epidural anesthesia with xylazine, bupivacaine and bupivacaine/xylazine mixture in West African Dwarf goats. *Israel Journal of Veterinary Medicine*. 2002; 57(2): 76-81.
24. Lawan AA, Falade FB, Adetunji A. Comparative evaluation of lignocaine and lignocaine-bupivacaine for lumbo-sacral epidural block in diazepam sedated West African dwarf goats. *Sokoto Journal of Veterinary Sciences*. 2019; 17(2): 27-32.
25. Ankalwar VR. Basics of Chronic Pain Management. *Vidarbha Journal of Internal Medicine*. 2022; 32(2): 120-128. doi: 10.25259/VJIM_16_2022
26. Grubb TL, Riebold TW, Crisman RO, Lamb LD. Comparison of lidocaine, xylazine, and lidocaine–xylazine for caudal epidural analgesia in cattle. *Veterinary Anesthesia and Analgesia*. 2002; 29(2): 64-68. doi: 10.1046/j.1467-2995.2001.00068.x
27. Kinjavdekar P, Amarpal GS, Aithal HP, Pawde AM. Physiologic and biochemical effects of subarachnoidally administered xylazine and medetomidine in goats. *Small Ruminant Research*. 2000; 38(3): 217-228. doi: 0.1016/S0921-4488(00)00161-9
28. Doherty TJ, Pascoe PJ, McDonell WN, Monteith G. Cardiopulmonary effects of xylazine and yohimbine in laterally recumbent sheep. *Canadian Journal of Veterinary*

Research. 1986; 50(4): 517.
29. Lawal FM, Adetunji A, Lawal FM. Evaluation of epidural anesthesia with lignocaine-xylazine mixture in ketamine-sedated cats. *Israel Journal of Veterinary Medicine*. 2009; 64(2): 47.
30. Saifzadeh S, Pourjafar M, Dalir-Naghadeh B. Caudal extradural analgesia with lidocaine, xylazine, and a combination of lidocaine and xylazine in the Iranian river buffalo (*Bubalus bubalis*). *Iranian Journal of Veterinary Surgery*. 2007; 2(3): 7-13.
31. Brohi RD, Kalhoro AB, Kachiwal AB, Kalhoro IB, Kalhoro DH, Ahmed S, Khan FA, Talpur HS, Zia-ur-Rehman ZU, Bhattaria D. Comparative effect of propofol and thiopentone sodium in sheep sedated with xylazine hydrochloride. *Pakistan Journal of Zoology*. 2019; 51(1): 1-7. doi: 10.17582/journal.pjz/2019.51
32. Udegbunam RI, Adetunji A. Comparison of three ketamine drug combinations for short term anesthesia in West African dwarf goats. *Agro-Science*. 2007; 6(2): 67-71. doi: 10.4314/as.v6i2.1573
33. Piantadosi S. Crossover designs, Chapter 20, In: *Clinical trials: A methodologic perspective*, 2nd Edn, Vol. 2 Piantadosi S, Balding DJ, Cressie NAC, Fisher NI, Johnstone IM, Kadane JB, eds. Hoboken, NJ: John Wiley and Sons, Inc., 2005; 515–527.
34. Siyasinghe NM, Sooriyarachchi MR. Guidelines for calculating sample size in 2×2 crossover trials: a simulation study. *Journal of the National Science Foundation of Sri Lanka*. 2011; 39(1). doi: 10.4038/JNSFSR.V39I1.2929
35. Gray PR, McDonell WN. Anesthesia in goats and sheep. I. Local analgesia. *Compendium on Continuing Education for the Practicing Veterinarian*, 1986, Vol. 8, No. 1, S33-S38.
36. Cruz ML, Luna SP, Clark RM, Massone F, Castro GB. Epidural anesthesia using lignocaine, bupivacaine or a mixture of lignocaine and bupivacaine in dogs. *Journal of Veterinary Anesthesia*. 1997; 24(1): 30-32. doi: 10.1111/j.1467-2995.1997.tb00265.x
37. Singh P, Pratap K, Amarpal, Kinjavdekar P, Aithal HP, Singh GR, Pathak R. Xylazine, ketamine and their combination for lumbar epidural analgesia in water buffalo calves (*Bubalus bubalis*). *Journal of Veterinary Medicine Series A.* 2006; 53(8): 423-431. doi: 10.1111/j.1439-0442.2006.00849.x
38. Umar MA, Gapsiso RH. Comparison of xylazne, lignocaine and combination of xylazine and lignocaine for epidural. *Nigerian Veterinary Journal*. 2008; 29(2): 15-19.
39. Araujo, M.A., Albuquerque, V.B., Deschk, M., Santos, G.G.F., Rodrigues, C.A., Oliva, V.N.L.S., Santos, P.S.P.. Cardiopulmonary and analgesic effects of caudal epidurally administered ropivacaine in cattle. *Veterinary anesthesia and Analgesia*. 2012; 39: 409-413. doi: 10.1111/j.1467-2995.2012.00726.x PMid:22574815 23
40. Shekidef MH, Saleh SY. Effects of epidural administration of ketamine/xylazine and ketamine/medetomidine combinations in dromedary camels (*Camelus dromedarius*). *Journal of Camel Practice and Research*. 2011; 18(2): 319-329.
41. Bromage PR. Spread of analgesic solutions in the epidural space and their site of action: a statistical study. *British Journal of Anesthesia*. 1962; 34(3): 161-178. doi: 10.1093/bja/34.3.161
42. Jones B, Kenward MG. Design and analysis of cross-over trials. *Chapman and Hall/CRC*; 2003. doi: 10.1201/9781420036091
43. Rush J, Stockler J. Local and regional anesthesia in food animals *Farm Animal Anesthesia: Cattle, Small Ruminants, Camelids, and Pigs*. 2022. 159-88. doi: 10.1002/9781119672661.ch8
44. De Rossi R, Bucker GV, Varela JV. Perineal analgesic actions of epidural clonidine in cattle. *Veterinary anesthesia and Analgesia*. 2003; 30(2): 63-70. doi: 10.1046/j.1467-2995.2003.00089.x
45. Lin HC, Trachte EA, DeGraves FJ, Rodgerson DH, Steiss JE, Carson RL. Evaluation of analgesia induced by epidural administration of medetomidine to cows. *American Journal of Veterinary Research*. 1998; 59(2): 162-167. doi: 10.2460/ajvr.1998.59.02.162
46. Fikes LW, Lin HC, Thurmon JC. A preliminary comparison of lidocaine and xylazine as epidural analgesics in ponies. *Veterinary Surgery*. 1989; 18(1): 85-86. doi: 10.1111/j.1532-950X.1989.tb01046.x
47. Grubb TL, Riebold TW, Huber MJ. Evaluation of lidocaine, xylazine, and a combination of lidocaine and xylazine for epidural analgesia in llamas. *Journal of the American Veterinary Medical Association*. 1993; 203(10): 1441-1444. doi: 10.2460/javma.1993.203.10.1441
48. Aithal HP, Pratap AK, Singh GR. Clinical effects of epidurally administered ketamine and xylazine in goats. *Small Ruminant Research*. 1997; 24(1): 55-64. doi: 10.1016/S0921-4488(96)00919-4
49. DeRossi R, Junqueira AL, Beretta MP. Analgesic and systemic effects of xylazine, lidocaine and their combination after subarachnoid administration in goats. *Journal of the South African Veterinary Association*. 2005; 76(2): 79-84.
50. Lemke KA. Anticholinergics and sedatives. *Lumb & Jones' Veterinary Anesthesia and Analgesia*. 2007; 208-209.
51. Dzikiti TB, Zeiler GE, Dzikiti LN, Garcia ER. The effects of midazolam and butorphanol, administered alone or combined, on the dose and quality of anesthetic induction with alfaxalone in goats. *Journal of the South African Veterinary Association*. 2014; 85(1): 1-8.
52. Cao JL, Ding HL, Zhang LC, Duan SM, Zeng YM. Pretreatment with midazolam suppresses morphine withdrawal response in mice and rats. *Acta Pharmacologica Sinica*. 2002; 23(8): 685-690.
53. Kyles AE, Waterman AE, Livingston A. Antinociceptive activity of midazolam in sheep. *Journal of Veterinary Pharmacology and Therapeutics*. 1995; 18(1): 54-60. doi: 10.1111/j.1365-2885.1995.tb00551.x
54. LW H. Patient monitoring and clinical measurement. *Veterinary Anesthesia*. 2001: 29-59.
55. Valverde A. Epidural analgesia and anesthesia in dogs and cats. *Veterinary Clinics of North America: Small Animal Practice*. 2008; 38(6): 1205-1230. doi: 10.1016/j.cvsm.2008.06.004
56. Mpanduji DG, Ndossi DG. Comparison of analgesia and cardio-pulmonary effects of epidural injection of pethidine and lidocaine in small East African goats. *Research Opinions, Animal Veterinary Science*. 2013; 3(2): 20-34.
57. Singh P, Pratap K, Kinjavdekar P, Aithal HP, Singh GR. Effects of xylazine, lignocaine and their combination for lumbar epidural analgesia in water buffalo calves (*Bubalus bubalis*). *Journal of the South African Veterinary Association*. 2005; 76(3): 151-158.
58. Zayed M, Mahmoud E, Khalil A, Salah M, Moustafa M, Youssef, M. Hassaneen A. Lumbosacral injection of lidocaine, detomidine and lidocaine–detomidine in goats: Anti-nociceptive effects and changes on haematobiochemical parameters. *Journal of Applied Animal Research*. 2020; 48(1): 57-62. doi: 10.1080/09712119.2020.1725520
59. DeRossi R, Zanenga NF, Alves OD, Carneiro RP, Ossuna MR, Jorge TP. Effects of caudal epidural ketamine and/or lidocaine on heifers during reproductive procedures: A preliminary study. *The Veterinary Journal*. 2010; 185(3): 344-346. doi: 10.1016/j.tvjl.2009.06.029
60. Aminkov B, Zlateva N. Epidural anesthesia for castration of the bitch. *Bulgarian Journal of Veterinary Medicine*. 2004; 7(2).
61. Lin HC, Purohit RC, Powe TA. Anesthesia in sheep with

propofol or with xylazine-ketamine followed by halothane. *Veterinary Surgery*. 1997; 26(3): 247-252. doi: 10.1111/j.1532-950X.1997.tb01494.x
62. Aziz MA, Martin RJ. α agonist and local anesthetic properties of xylazine. *Zentralblatt für Veterinärmedizin Reihe A*. 1978; 25(3): 181-188. doi: 10.1111/j.1439-0442.1978.tb00918.x
63. Butterworth JF, Strichartz GR. Molecular mechanisms of local anesthesia: A review. *Anesthesiology*. 1990; 72: 711–734. doi: 10.1097/00000542-199004000-00022
64. Maze M, Tranquilli W. Alpha-2 adrenoceptor agonists: Defining the role in clinical anesthesia. *Journal of the American Society of Anesthesiologists*. 1991; 74(3): 581-605. doi: 10.1097/00000542-199103000-00029
65. Egbe-Nwiyi TN, Nwaosu SC, Salami HA. Haematological values of appararently healthy sheep and goats as influenced by age and sex in arid zone of Nigeria. African Journal of Biomedical Research. 2000; 3(2):109-15.
66. Olaifa AK, Olatunji-Akioye AO, Agbaje LO, Olatunji-Akioye AO. Distal paravertebral nerve block effects on West African dwarf goat hematology and physiology. *Israel Journal of Veterinary Medicine*. 2009; 64(4): 128.
67. Jean GS, Skarda RT, Muir WW, Hoffsis GF. Caudal epidural analgesia induced by xylazine administration in cows. *American Journal of Veterinary Research*. 1990; 51(8): 1232-1236. doi: 10.2460/ajvr.1990.51.08.1232
68. Lin HC, Trachte EA, DeGraves FJ, Rodgerson DH, Steiss JE, Carson RL. Evaluation of analgesia induced by epidural administration of medetomidine to cows. *American Journal of Veterinary Research*. 1998; 59(2): 162-167. doi: 10.2460/ajvr.1998.59.02.162
69. Waterman AE, Livingston A, Amin A. Analgesic activity and respiratory effects of butorphanol in sheep. *Research in Veterinary Science*. 1991; 51(1): 19-23. doi: 10.1016/0034-5288(91)90024-I
70. Skarda RT. Local and regional anesthesia in ruminants and swine. *Veterinary Clinics of North America: Food Animal Practice*. 1996; 12(3): 579-626. doi: 10.1016/S0749-0720(15)30390-X
71. Ruffolo Jr RR, Nichols AJ, Stadel JM, Hieble JP. Pharmacologic and therapeutic applications of alpha2-adrenoceptor subtypes. *Annual Review of Pharmacology and Toxicology*. 1993; 33(1): 243-279. doi: 10.1146/annurev.pa.33.040193.001331
72. MacDonald E, Scheinin H, Scheinin M. Behavioural and neurochemical effects of medetomidine, a novel veterinary sedative. *European Journal of Pharmacology*. 1988; 158(1-2): 119-127. doi: 10.1016/0014-2999(88)90260-9.