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Comparative antinociceptive and sedative effects of epidural romifidine and xylazine in dromedary Camels (*Camelus dromedarius*)

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Abstract

In this study, the pain-relieving and calming effects of giving romifidine and xylazine through an epidural in camels were compared. Twenty-one adult camels (9 non-pregnant females and 12 intact males) weighing between 400–450 kg were randomly divided into three equal groups. Each group received one of the following treatments: an equal volume of sterile saline, 0.17 mg/kg of xylazine, or 50 g/kg of romifidine. All of the treatments were put directly into the sacrococcygeal space after being diluted in 0.9% sterile saline solution until the final volume was 20 ml. Before treatment and then at 5, 10, 15, 30, 60, 90, 120, 150, and 180 min after administration, the perineal analgesia, sedation, and degree of ataxia were evaluated. At these same times, rectal temperature (RT), heart rate (HR), and respiration rate (RR) were simultaneously measured. Epidural administration of romifidine and xylazine resulted in varying degrees of sedation, ranging from mild to deep, alongside complete antinociception affecting the perineum, inguinal area, and flank. This effect extended distally to the coronary band of the hind limbs and cranially to the thoracic region. After romifidine, analgesia started more quickly than with xylazine (6 ± 1.05 vs. 14.17 ± 0.83). The duration of both antinociceptive for romifidine was substantially longer than that of xylazine (159 ± 6.38 vs. 63.33 ± 2.47). The onset time of sedation was substantially shorter after romifidine (6.8 ± 0.83 min) compared to xylazine (10.8 ± 0.83 min). Romifidine's sedative effect lasted longer than xylazine's (149.17 ± 4.16 vs. 108.33 ± 1.05 min). At every study measurement point, the romifidine and xylazine-treated groups showed negligible RT, HR, and RR changes. **Conclusion:** Romifidine or xylazine may be a reliable, durable, and economical method for epidural anesthesia in camels undergoing standing surgery, as romifidine has a faster onset and longer antinociceptive effect. Therefore, epidural romifidine could be a more effective treatment option for immediate postoperative pain.

Keywords Anti-nociception, *Camelus dromedaries*, Epidural, Romifidine, Xylazine, Sedation

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Introduction

The dromedary camel (*Camelus dromedaries*) is characterized by a specialized locomotor mechanism that enhances its performance as a racing animal. Dromedary camels are primarily distributed in tropical climates around the world and hold considerable importance in the socio-economic contexts of nomadic societies [1]. Although camels are crucial to the livelihoods of human societies in tropical areas, there has been a strikingly low level of systematic investigation and expertise focused on this species. A variety of veterinary anesthesia principles that apply to different species are also relevant to camelids. However, it has been found that camels may be more vulnerable to toxicity from some medications at concentrations normally used for other ruminants [2, 3]. Although general anesthesia is often employed in a variety of surgical operations on a wide range of animal species, camel surgeons face considerable difficulties when dealing with it. When compared to regional anesthesia, the hazards of aspiration pneumonia and suffocation are the main worries, and they exceed the expense and the requirement for specific equipment [4].

Caudal epidural analgesia is increasingly recognized in veterinary practice as a substantial alternative to general anesthesia for various surgical and obstetrical procedures in ruminants, particularly in field situations. Moreover, caudal epidural analgesia is capable of delivering effective analgesia with superior therapeutic outcomes in addressing pre- and postoperative pain in the hind limbs, pelvic region, and caudal areas of these animals [5]. This effectiveness has contributed to a growing clinical interest in the use of this technique in veterinary anesthesia over the last decade [6].

Caudal epidural injection of local anesthetics, typically 2% lidocaine solution, is commonly used in camels for surgical procedures on the tail, anus, rectum, perineum, and caudal portions of the urogenital system [7, 8]. However, the duration of analgesia provided by most local anesthetics is relatively short, often necessitating re-administration to complete longer surgical interventions. Additionally, these anesthetics may cause weakness in the hind limbs and, in some situations, the animal because they non-specifically block sensory, motor, and sympathetic nerve fibers [9]. For interventions that necessitate extended analgesia, the extradural or epidural administration of long-acting analgesics is often preferable. This category of drugs includes α-2 adrenoceptor agonists, dissociative anesthetics, and steroidal and non-steroidal agents, along with opioids that specifically target sensory fibers. This approach yields significant analgesic effects while minimizing the risk of impairing motor function in the pelvic limbs [10]. These medications can be administered individually or in various combinations [11].

Epidural α-adrenergic agents are extensively utilized in veterinary medicine for chemical restraint, owing to their ability to selectively block sensory pathways while sparing motor and autonomic neurons from adverse depression. Consequently, these agents may present benefits compared to local anesthetics, such as reduced hind limb weakness and an extended duration of action [11, 12]. As selective α-2 adrenoceptor agonists, romifidine and xylazine demonstrate analgesic effects along with systemic actions in numerous animal species. These medications have been utilized by epidural or spinal administration in ruminants, both large and small [13–16].

Romifidine is a derivative of imidazolidine that acts as an α-2 agonist. It has been utilized to treat systemic and analgesic symptoms in a variety of animal species, including horses, dogs, goats, and cattle. When given to cattle systemically, romifidine appears to have similar effects to xylazine, with faster and longer-lasting analgesia [17]. When romifidine was administered epidurally to adult cattle, the tail, anus, perineum, vulva, and inguinal region all had an antinociceptive response [20]. Analgesia has been shown to reach the thoracic regions and the coronary band of the hind limbs [24]. With mild to moderate sedation at 30 and 40 µg/kg doses and severe sedation at the 50 µg/kg dose after epidural administration, a dose-dependent sedative effect was documented [24]. In goats, romifidine (50µg/kg) administered epidurally produced sedative and analgesic effects that lasted longer than those of xylazine (26). Similar levels of full caudal analgesia are produced in camels when lidocaine and xylazine (0.22 mg/kg and 0.17 mg/kg) are administered together as opposed to when either drug is administered alone (15). As far as the authors are aware, the application of epidural analgesia in camels utilizing xylazine and romifidine has not been previously documented. Thus, the primary aim of this research was to assess and compare the antinociceptive and sedative effects of romifidine and xylazine when administered epidurally in camels.

Materials and methods

The camel used

Twenty-one adult, healthy dromedary camels (9 non-pregnant females and 12 intact males) were used for this study. They were between the ages of 5 and 7 years and weighed between 400 and 450 kg. All camels were deemed healthy based on hematological and clinical screening results. Moreover, five camels with unsatisfactory health, body condition scores below 3, an inaccessible sacrococcygeal space, a history of epidural injections

or local blocks in the perineal region, or skin conditions in the area of interest were excluded. Each animal was kept in its corral. Every camel was fed grass hay that had been enhanced with concentrate. Before the trial, they were given unrestricted access to water for 24 h while their feed was stopped. The present study was carried out following the standard rules toward animals. The camels were collected immediately from their owners, and informed consent from the owners has been properly obtained. The anatomical terms were used based on Nomina Anatomica Veterinaria [18].

Experimental study design

All trials were carried out outdoors in a peaceful setting with natural daylight and a target temperature of up to 27 degrees. Seven camels were randomly allocated to each of the three treatment groups, consisting of three non-pregnant females and four males. All camels were controlled in sternal recumbency. Before being evaluated, camels were given twenty minutes in the stall to get used to their new environment. Each camel was weighed before the experiment started, and measurements were made of its body temperature with a digital thermometer, heart rate (HR) (number of beats/min), and respiration rate (RR) as number of chest movements/min, and ruminal contractions was assessed by auscultation.

The sacrococcygeal region was cleaned with povidone-iodine after the hair was shaved. Three treatments of the same volumes were given to each group over a period of around 30 s into the epidural space. One of the following was used to treat each group: An equal volume of sterile saline (group 1), 0.17 mg/kg of xylazine (group 2) [15], or 50 µg/kg of romifidine (group 3) [19]. Utilizing an 18-gauge, 4-cm hypodermic needle, all treatments were diluted in 0.9% sterile normal saline solution to yield an overall dose volume of 20 ml. These were then injected precisely into the epidural space between the first and second coccygeal vertebrae (the first intercoccygeal epidural space), as clarified in (Fig. 1A). Palpating the depression between the first and second coccygeal vertebrae and moving the tail up and down allowed for the identification of the space. Guided anteriorly and ventrally, the needle was entered to a depth of 2 cm at a 45° angle to the skin's surface. The hanging drop technique was used for identifying negative pressure; a small volume of air (2–3 ml) was easily injected, and there was no obstacle to the injection, which verified that the needle was positioned correctly [20]. A steady injection of the solution into the epidural area was made after the needle was placed. The individual administering each epidural was ignorant of the protocols. The camels were lifted, led into a chute, and watched for any negative effects of the medication once it was administered. A pinprick test, which uses a 22-gauge, 2.5-cm long hypodermic needle to pierce the skin into the deep tissues at specific anatomical locations, such as the base of the tail, anus, vulva, perineum, caudal aspect of the thigh, and inguinal area, was used to assess antinociception. Bilateral needle insertions were made at slightly varied points for every time point. They used a povidone-iodine solution to treat the skin prick injuries. When pinpricks produced no response, pinching with artery forceps was employed to determine a high level of analgesia. Pinching was solely done on the perineum and inguinal area.

The extent of antinociception was assessed using a rating system [16]: 0 to 3: 0, no analgesia (forceful reaction to an unpleasant event, such as the animal's limb moving violently); 1, mild analgesia (mild reaction, like tilting the head in the direction of the stimulus); 2, moderate analgesia (extremely weak and inconsistent reaction); and 3,

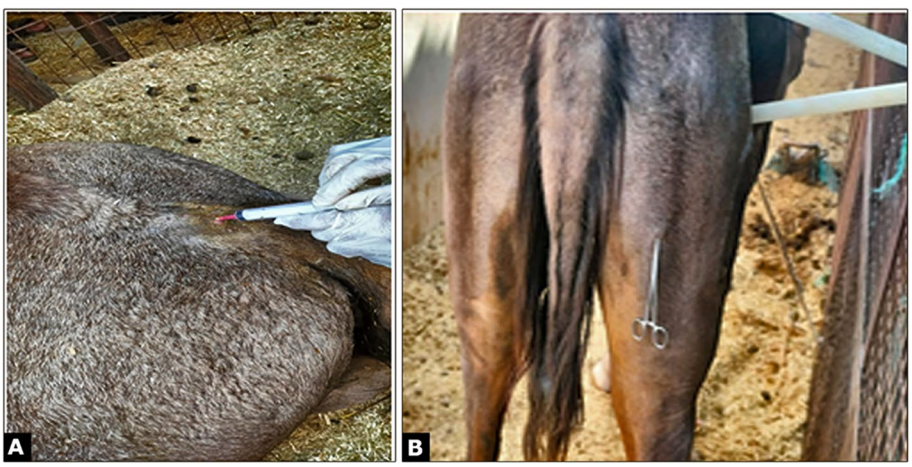

Fig. 1 Gross image describing the epidural administration of romifidine (View A) and describing the pinching using artery forceps showing a complete perineal analgesia post-epidural injection of romifidine (View B) in camels (*Camelus dromedarius*)

complete analgesia (no reaction to an undesirable stimulation.). The time to the beginning of perineal analgesia was measured every minute after the epidural injection by assessing the animal's responsiveness to pinpricks and artery forceps pinching. The perineal analgesia duration (in minutes) was calculated as the period between the absence and return of a reaction to pinprick and pinching stimuli.

The extent of sedation was assessed using a rating system [16]: 0 = no sedation (awake, attentive, retaining typical positions of the head with their ear, eyelids, lips, and tongue; and the neck, and responsive to striking on a metal bar near the animal's head; 1 = mild sedation (diminished attentiveness, minor sink of the head, ear, and lips, palpebral ptosis, protrusion of the tongue out the mouth, and somewhat diminished responsiveness to striking on a metal bar near to the animal's head.); 2 = moderate sedation (tardiness, a noticeable lowering of the head, ear, and lips, increased protrusion or hanging of the tongue out of the mouth, neck deviation, and sporadic response to striking on a metal bar near to the animal's head.); 3 = deep sedation (noticeable tardiness, lowering of the head and lips, palpebral ptosis, deviation of the neck, prominent ear tip separation and lower ear carriage, and absence of responsiveness to striking on a metal bar near the animal's head).

The period between epidural administration and the start of sedation was designated the sedation onset time. The sedation duration (in minutes) was calculated as the period from the beginning of sedation to the recovery of the sedation score to zero.

Ataxia was assessed via a basic 4-point rating system [16]: 0 = normal, 1 = slight or mild (mild or irregular wide posture of the rear legs, slight tilting or stumbling, yet capable of walking); 2 = moderate (noticeable falling, frequent broad posture of rear legs, frequent fetlock knuckling, walking with considerable incoordination, trying to lie down but readily convinced to stand); or 3 = severe (attaining a cush position and incapable of being lifted). All animals' anti-nociception, ataxia, and sedation were evaluated by the identical observer, who was ignorant of the treatments being given.

Time table

Baseline values were evaluated before drug administration. Heart rate, RR, rectal temperature (RT), Ruminal contraction, lacrimation, salivation, urination, analgesia, sedation, ataxia, and tail flaccidity were measured before (baseline, 0), at 5, 10, 15, 30, 45, 60, 90, 120, 150 and 180 min after treatments. The experimental animals were clinically monitored for one week after treatment.

Statistical analysis

Software for statistical analysis (SPSS Inc., Chicago, IL, USA) was used to analyze all of the data. Initially, the data were tested for normality with the Shapiro–Wilk normality test. The statistical differences of the non-parametric data, including analgesia, sedation, and ataxia, were detected at different time points with the Kruskal–Wallis test with post-hoc Dunn's multiple comparison tests. For parametric data, including HR, RR, and RT, the time and treatment effects were evaluated using a general linear model with repeated measures ANOVA. To assess interactions within groups and verify interactions across time, the Wilks-Lambda test was used. Romifidine and xylazine were tested for their effects on the onset and duration of analgesia, sedation, ataxia, and tail flaccidity using an unpaired t-test; results were shown as mean ± SD or median (range), with differences regarded as significant at $P < 0.05$.

Results

All experimental camels accepted the epidural injections well, and the procedures were simple. According to treatment-time interaction, there was a notable difference in the level of antinociception among the three treatments and over time. The nociceptive reflexes of every camel that received an epidurally administered injection of normal saline did not differ significantly. Complete perineal analgesia was achieved with epidural treatment with romifidine (Fig. 1B) and xylazine as opposed to normal saline.

After romifidine, analgesia started more quickly than with xylazine (6 ± 1.05 vs. 14.17 ± 0.83), as clarified in Table 1. The analgesic duration for romifidine was substantially longer than that of xylazine (159 ± 6.38 vs. 63.33 ± 2.47). When romifidine was administered

Table 1 Onset and duration of analgesia (minutes), sedation, ataxia, and tail flaccidity (mean ± standard deviation) after epidural injection of xylazine and romifidine in camels

Groups	Analgesia		sedation		Ataxia		Tail flaccidity	
	onset	Duration(min)	onset	Duration(min)	Onset	Duration(min)	onset	duration
Xylazine	14.17 ± .83[a]	63.33 ± 2.47[b]	10.8 ± .83[a]	108.33 ± 1.05[b]	10.8 ± .83[a]	83.3 ± 3.3[b]	14.17 ± .83[a]	110 ± 4.9[b]
Romifidine	6 ± 1.05[b]	159 ± 6.38[a]	6.8 ± 0.83[b]	149.17 ± 4.16[a]	7.5 ± 1.2[b]	132.5 ± 7.16[a]	6.6 ± 5.05[b]	162.5 ± 5.6[a]

[a,b] Means with different superscript letters in the same column are significantly different at $P < 0.05$

epidurally, the analgesia score was considerably higher ($P < 0.05$) than when xylazine was administered at 5, 10, 120, and 150 min after treatment. The analgesic effects of romifidine peaked between 10 and 150 min after the drug was administered. Between 15 and 90 min after delivery, xylazine had its most analgesic effects (Table 2).

Before receiving the three treatments by epidural injection, all camels responded to noxious stimulation with a score of 0 (no analgesia). After romifidine and xylazine were administered epidurally, an elevated threshold to skin prick stimulation (full analgesic effect; pain score 3) was attained roughly 10 and 15 min later, respectively. As time went on, the analgesic impact significantly increased ($P < 0.01$).

When compared to animals given normal saline, all animals treated with romifidine and xylazine exhibited substantial alterations in their sedation scores ($P < 0.05$). When compared to xylazine (10.8 ± 0.83 min), the onset time of sedation was substantially ($P < 0.05$) shorter after romifidine (6.8 ± 0.83 min). Depending on the treatment, the sedation scores substantially changed over time. Romifidine's sedative effect (Fig. 2) lasted longer than xylazine's (149.17 ± 4.16 vs. 108.33 ± 1.05 min). The greatest sedative effect (deep sedation, score = 3) happened 10–90 min after romifidine was administered epidurally and 15–45 min after xylazine was administered.

At 10–120 and 10–90 min after romifidine and xylazine treatments, respectively, all animals were ataxic (Table 2). Both medications caused mild ataxia (scoring

Table 2 Analgesia, sedation and ataxia scores (median and range) after epidural injection of normal saline or romifidine and xylazine in camels

Time post administration (minutes)											
	T0	**T5**	**T10**	**T15**	**T30**	**T45**	**T60**	**T90**	**T120**	**T150**	**T180**
Analgesia scores											
Saline	0 (0–0)^{a}	0 (0–0)^{b}	0 (0–0)^{b}	0 (0–0)^{b}	0 (0–0)^{b}	0 (0–0)^{b}	0 (0–0)^{b}	0 (0–0)^{b}	0 (0–0)^{b}	0 (0–0)^{b}	0 (0–0)^{b}
Romifidine	0 (0–0)^{a}	1 (0–2)^{a}	3 (3–3)^{a}	3 (3–3)^{a}	3 (3–3)^{a}	3 (3–3)^{a}	3 (3–3)^{a}	3 (3–3)^{a}	3 (3–3)^{a}	2 (2–3)^{a}	0 (0–1)^{a}
Xylazine	0 (0–0)^{a}	0 (0–0)^{b}	0 (0–1)^{b}	3 (1–3)^{a}	3 (3–3)^{a}	3 (3–3)^{a}	3 (3–3)^{a}	3 (3–3)^{a}	0 (0–1)^{b}	0 (0–0)^{b}	0 (0–0)^{b}
Sedation scores											
Saline	0(0–0)^{a}	0(0–0)^{b}	0(0–0)^{b}	0(0–0)^{b}	0(0–0)^{b}	0(0–0)^{b}	0(0–0)^{c}	0(0–0)^{c}	0(0–0)^{b}	0(0–0)^{b}	0(0–0)^{b}
Romifidine	0(0–0)^{a}	1(0–2)^{a}	3(3–3)^{a}	3(3–3)^{a}	3(3–3)^{a}	3(3–3)^{a}	3(3–3)^{b}	3(3–3)^{a}	2(2–3)^{a}	1.5(1–2)^{a}	1(1–2)^{a}
Xylazine	0(0–0)^{a}	0(0–0)^{b}	0(0–1)^{b}	3(1–3)^{a}	3(3–3)^{a}	3(3–3)^{a}	1.5(1–2)^{a}	1(1–1)^{b}	0(0–0)^{b}	0(0–0)^{b}	0(0–0)^{b}
Ataxia scores											
Saline	0(0–0)^{a}	0(0–0)^{a}	0(0–0)^{b}	0(0–0)^{b}	0(0–0)^{b}	0(0–0)^{b}	0(0–0)^{b}	0(0–0)^{b}	0(0–0)^{b}	0(0–0)^{b}	0(0–0)^{a}
Romifidine	0(0–0)^{a}	0(0–1)^{a}	1(0–1)^{a}	1(1–1)^{a}	1(1–3)^{a}	1(1–2)^{a}	1(1–2)^{a}	1(1–2)^{a}	1(1–1)^{a}	0.5(0–1)^{a}	0(0–1)^{a}
Xylazine	0(0–0)^{a}	0(0–0)^{a}	1(0–1)^{a}	1(1–1)^{a}	1(1–3)^{a}	1(1–2)^{a}	1(1–2)^{a}	1(1–2)^{a}	0(0–1)^{b}	0(0–0)^{b}	0(0–0)^{a}

$^{a,b,\ c}$Medians with different superscript letters in the same column are significantly different at $P < 0.05$

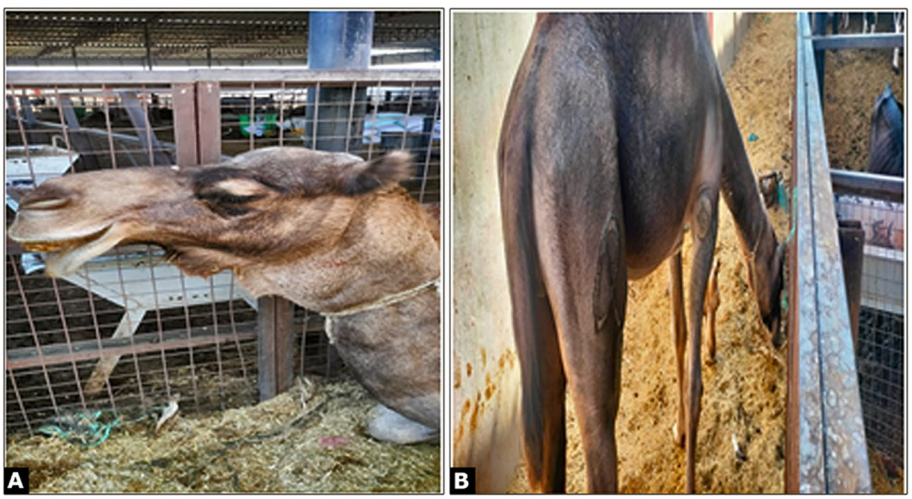

Fig. 2 Gross image (Views A-B) describing the sedative effect of romifidine after epidural administration in camels

Table 3 Heart rate (Heart beat/min), Respiratory rate (respiratory cycle/min) and Rectal temperature (°C) (mean and standard deviation) after epidural injection of normal saline or romifidine and xylazine in camels

Time post administration (minutes)											
	T0	**T5**	**T10**	**T15**	**T30**	**T45**	**T60**	**T90**	**T120**	**T150**	**T180**
Heart rate											
Saline	41.2 ± 3.6	41.3 ± 3.7	40.8 ± 2.8	40.7 ± 3.5	41 ± 3.5	40.3 ± 3	40.5 ± 3.7	41.3 ± 3.8	41 ± 3.5	40.8 ± 3.8	41.3 ± 3.4
Romifidine	41 ± 3.7	40.2 ± 3.8	40 ± 4.3	39.5 ± 3.6	39.3 ± 4.03	38.5 ± 4.1	38.2 ± 4	36.8 ± 3.9	37.8 ± 4.2	39 ± 4	39.8 ± 4.3
Xylazine	40 ± 5.2	40.3 ± 5.1	39.6 ± 5.5	39.2 ± 5.6	38.7 ± 5.8	38.3 ± 5.2	37.2 ± 5.5	37.6 ± 5.6	39.3 ± 6.7	38.6 ± 5.6	39 ± 5
Respiratory rate											
Saline	18.2 ± 4.16	17.3 ± 3.6	19 ± 4.4	19.2 ± 4.2	18 ± 3.9	19.6 ± 3.8	19.6 ± 3.8	18.2 ± 3.4	19.5 ± 3.1	19 ± 2.9	18.8 ± 4.1
Romifidine	18.1 ± 4.17	18.6 ± 3.4	17.5 ± 4.8	16.8 ± 4.5	15.3 ± 4.7	15.6 ± 3.9	15 ± 4.6	13.5 ± 4.5	16.2 ± 3.6	16 ± 3.7	16.3 ± 3.5
Xylazine	18.3 ± 3.8	18.7 ± 3.2	18.6 ± 3.5	16.82 ± 2.9	16.3 ± 3.9	15.7 ± 3.7	15.3 ± 3.6	16.3 ± 3.7	16.8 ± 3.4	16.3 ± 4.1	17.6 ± 3.3
Rectal temperature											
Saline	37.50 ± 0.48	37.38 ± 0.72	37.65 ± 0.51	37.6 ± 0.45	37.7 ± 0.73	37.76 ± 0.73	37.6 ± 0.77	37.6 ± 0.50	37.6 ± 0.51	37.4 ± 0.47	37 ± 0.6
Romifidine	37.68 ± 0.6	37.65 ± 0.71	37.38 ± 0.76	37.41 ± 0.63	37.21 ± 0.58	37.03 ± 0.59	36.70.66	36.6 ± 0.67	36.7 ± 0.76	36.80.42	37.2 ± 0.42
Xylazine	38.03 ± 0.54	37.9 ± 0.55	37.76 ± 0.55	37.55 ± 0.62	37.50 ± 0.51	37.25 ± 0.53	37.03 ± 0.60	36.9 ± 0.6	37.2 ± 0.55	37.3 ± 0.5	37.6 ± 0.63

1) in camels when administered epidurally (Table 2). Nevertheless, throughout the research, there was no indication of ataxia in the control animals. Romifidine's flaccidity effect lasted longer than xylazine's (162.5 ± 5.6 vs. 110 ± 4.9 min). As a result, the flaccidity effect persisted for at least 180 min after romifidine treatment and 150 min after xylazine administration.

There were no discernible variations across treatments, and the RT, HR, and RR were always constant when compared to the baseline value (Table 3). Following the medication's epidural injection, no negative side effects were seen. The cases' follow-up revealed no indications of neurological damage or infection at the needle puncture site.

When both medications were administered epidurally, the total number of ruminal contractions in five minutes decreased significantly 30–60 min after the injection ($P < 0.001$). After romifidine and xylazine were administered epidurally, mild lacrimation and salivary drooling were seen. Furthermore, every camel used both medications to urinate multiple times, ranging from two to four times. Clinical signs of ruminal tympany and penile prolapse were absent in all treated animals. All of the treated camels were eating and drinking normally 24 h following the epidural injection.

Discussion

Camels are challenging to intubate because of their narrow oral cavity, making them unsuitable for general anesthesia and increasing the risk of complications like pneumonia and regurgitation [21]. Therefore, epidural anesthesia may be an appropriate anesthetic technique for camels. In farm animal species, caudal epidural anesthesia is a popular regional anesthetic procedure where anesthetic drugs are administered into the epidural space to manage neuroaxial pain. This method successfully hinders sensory and motor spinal nerve roots of the caudal regions of the animals, allowing for various surgeries in the caudal regions to be performed [22]. However, several anesthetic drugs, like dissociative anesthetics, steroids, and opioids, suppress sensory fibers for effective pain relief; α-2 adrenergic receptor agonists have recently become widely used in animals [23, 24]. The degree and duration of sedation, analgesia, and cardiorespiratory effects are all impacted by the medicines' binding specificity at the α-2 adrenergic receptors [19].

Romifidine is an α-2 adrenergic receptor agonist medication derived from imidazolidine. In addition to epidural administration, it can also be given intramuscularly and intravenously to horses and both small and large ruminants [25, 26]. Although α2 adrenergic receptor agonists are frequently used in farm animal species, little research has been published on their use for epidural analgesia in dromedary camels.

The significant perineal analgesia noted in this investigation after epidural injection of both romifidine and xylazine aligns with the findings of Marzok, et al. [16] and his colleagues, who reported a similar finding in camels after epidural administration of romifidine, and with Molaei, et al. [15], who noted significant analgesia in the caudal area of camels after epidural administration of xylazine. Epidural administration of α-2 adrenoceptor agonist's xylazine and romifidine stimulates α-2 adrenoceptors in the pre- and postsynaptic areas of the spinal cord's dorsal horn. This process reduces the transmission of pain signals and decreases the release of norepinephrine and substance P, ultimately enhancing anti-nociceptive effects. According to this study, romifidine produces analgesia more quickly than xylazine, which is in line with Korittum [27] findings that epidural romifidine in goats reduces pain more quickly than xylazine. The prolonged analgesia provided by romifidine in comparison to xylazine, as demonstrated in this study, corresponds with results from previous research on small and large animals. Romifidine, a potent α-2 adrenoceptor agonist, and demonstrates double selectivity for α-2/α-1 compared to xylazine [28]. As a result, epidural romifidine provides longer-lasting analgesia than xylazine.

Sedation is recommended for nervous and vigorous camels receiving clinical assessment and surgical procedures in veterinary facilities to minimize stress and reduce injury risk [26, 29]. In addition to its analgesic effect, in clinical camel treatment, α-2 agonists are commonly utilized to induce sedation [6, 29]. Both the romifidine and xylazine groups had considerable sedation, which began at 6.8 ± 0.83 and lasted for 149.17 ± 4.16 in the romifidine group, whereas in the xylazine group, sedation commenced at 10.8 ± 0.83 and persisted for 108.33 ± 1.05 min. α-2 adrenergic agonists mainly induce sedation by reducing the function of noradrenaline-producing cells in the locus coeruleus (LC), a part of the brain found in the pons and lower brainstem. This decrease in LC function results in less noradrenaline reaching upper brain areas, ultimately causing a calming impact [30]. The sedative effects of these drugs are also enhanced by the existence of postsynaptic α-2-adrenergic receptors in the frontal cortex, which inhibit cortical activity, contributing to calming effects. Furthermore, they can modulate neurotransmitter release and reuptake by taking action on presynaptic α-2 adrenergic receptors on both noradrenergic and non-noradrenergic neurons, regulating arousal and alertness [30]. The rapid onset sedative effect of romifidine compared to xylazine reported in this study may be attributed to its high lipid solubility [31]. Romifidine via the epidural route also showed prolonged sedation compared to xylazine. This

could be because xylazine is metabolized and eliminated more quickly after absorption [32].

In the current experimental research, camels treated with romifidine and xylazine displayed different levels of ataxia, ranging from mild to extreme. Ataxia may arise from the mixed systemic impacts of muscle relaxation and sedation induced by α-2 agonists [33]. These results conflict with those of Molaei, et al. [15], who found that camels only experienced minor ataxia after receiving epidural anesthesia, but they are in line with Marzok, et al. [16]'s findings that camels experienced mild to moderate ataxia following the injection of romifidine via epidural.

In the current experimental study, camels given xylazine and romifidine epidurally developed tail flaccidity. Such results may be explained by motor fiber blockage [34]. By blocking intraneuronal impulse transmission at the central nervous system level, α-2 agonists have been shown to have an effective muscle relaxant effect. According to a previous study, xylazine and romifidine have similar local anesthetic-like effects on spinal nerve roots. When injected epidurally, they have a local inhibitory impact on A-α fibers, which are thought to control motor function, according to Butterworth and Strichartz [35], Chambers [36].

There was also a notable reduction in camel ruminal contractions following romifidine and xylazine administration. Buffalos have also shown a comparable reduction of romifidine-induced ruminal contractions [37]. This study did not find significant tympany, even though α-2 agonists are linked to decreased motility and a relaxing impact on the gastrointestinal system [38].

Both xylazine and romifidine administered epidurally resulted in a constant heart rate, indicating that there is no significant systemic impact on paravertebral sympathetic fibers, as previously noted [39]. Following epidural xylazine, similar outcomes have been seen in camels [40] and donkeys [41]. On the other hand, camels [15] and buffalos [6] showed a notable reduction in heart rate after receiving epidural xylazine and romifidine, respectively. Bradycardia after receiving an α-2 adrenoceptor agonist may be caused by central stimulation of the vagus nerve [38]. Both drugs had no significant influence on respiration rates or rectal temperatures in treated camels after being administered epidurally. Similar effects were seen following epidural xylazine in camels [40] and romifidine in buffalos [37]. However, epidural treatment of xylazine resulted in a considerable decrease in respiration rate in camels.

In this investigation, mild salivary drooling was seen. Buffalos that utilized romifidine epidurally concurred with these findings of Marzok and El-khodery [37]. Conversely, there were noticeable increases in salivation in cattle that were given romifidine or detomidine [42]. Furthermore, each camel that used both kinds of medications urinates two to four times. This may be explained by the way α-2 agonists suppress the antidiuretic hormone [38].

The fact that the authors only utilized one dosage of xylazine and romifidine is a drawback of this study. First, it is not possible to evaluate the dose-dependent sedative and analgesic effects of each medication in camels due to this characteristic of the study design. Second, the pharmacokinetics of these medications in camels are unknown, which could make it challenging to recognize and clarify some of the drugs' clinical effects. Third, the small number of camels may influence how we interpret our results. Consequently, findings based on a more thorough comprehension of xylazine and romifidine in camels will yield a more tangible conclusion. Furthermore, the effects of intramuscular or intravenous epidural injections have not been compared in this investigation. As a result, the mechanism of action's full explanation remains dubious.

Conclusion

This study compared the antinociceptive and sedative effects of epidural administration of romifidine and xylazine in camels. Romifidine or xylazine may be a reliable, durable, and economical method for epidural anesthesia in camels undergoing standing surgery. Romifidine has a faster onset and longer antinociceptive effect than xylazine. Therefore, epidural romifidine may show promise as an analgesic that provides superior therapeutic advantages in the treatment of acute postoperative pain in camels.

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Data availability
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The present study was carried out in accordance with the standard rules, guidelines, and regulations set forth by the Animal Ethics Committee and under the protocol number (approval code: KFS-IACUC/251/2025) of the Faculty of Veterinary Medicine, Kafrelsheikh University, and complied with the regulations of the National Committee for Research regarding the care and use of animals for scientific purposes. All methods were performed in accordance with relevant guidelines and regulations from the Basel Declaration and the International Council for Laboratory Animal Science (ICLAS). The study was conducted in accordance with the local legislation and institutional requirements. The source of the camels utilized in this study was obtained directly from their respective owners. In adherence to ethical standards, we confirm that informed consent from the owner has been duly obtained. All methods are reported in accordance with ARRIVE guidelines.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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