



Comparison of Lidocaine, Xylazine, and a Combination of Lidocaine and Xylazine for Caudal Epidural Analgesia in Dromedary Camels

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Abstract

Objective- This study was performed to investigate the analgesic effects of lidocaine, xylazine and lidocaine/xylazine combination in epidural anesthesia in dromedary camels.

Design- Experimental Study

Animals- Fifteen healthy immature dromedary camels

Methods- The camels were randomly designed in 3 equal groups. In group L: lidocaine 2% (0.22 mg/kg), in group X: xylazine 2% (0.17 mg/kg), and in group LX: a combination of lidocaine 2% (0.22 mg/kg) and xylazine 2% (0.17 mg/kg) were injected into the first intercoccygeal epidural space. Analgesia, sedation, ataxia, and effect on cardiopulmonary, rectal temperature were recorded at different intervals before (baseline) and after the drug administration.

Results- Epidural lidocaine, xylazine and their combination produced analgesia in the tail, anus and perineum. Onset time of perineal analgesia in groups L and LX was significantly shorter than group X. Duration of complete perineal analgesia in group X and LX was significantly longer than group L. Mild to moderate sedation was observed in groups X and LX, whilst the camels in group L were alert and nervous during the study. Ataxia was observed in all test subjects and was more severe in group L and LX. Significant depression in heart rate, respiratory rate, and rectal temperature values were observed in groups X and LX in some measurement points of the study.

Conclusion and Clinical Relevance- According to the results of present study, it could be concluded that a combination of lidocaine and xylazine administered

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epidurally to dromedaries produces an effective, safe, with more rapid onset of longer perineal analgesia, when compared with either agent alone.

Key Words- Epidural, Lidocaine, Xylazine, Dromedary Camels.

Introduction

Caudal epidural analgesia can be used to perform surgery of the perineum, rectum, and vagina in standing animals and most commonly produced by local anaesthetics (usually lidocaine 2% solution) injected into the caudal epidural space.¹ Lidocaine provides analgesia of relatively short duration and may necessitate re-administration of the agent to allow completion of the procedure. In addition, local anesthetic agents indiscriminately block motor, sensory, and sympathetic fibers causing ataxia, hind limb weakness, and occasionally recumbency.² Epidural and intrathecal administration of agents with greater duration of action may be more appropriate for procedures requiring long duration analgesia. These agents include opioids and alpha-2 adrenergic agonists which selectively block sensory fibers, thereby providing significant analgesia with decreased likelihood of rear limb dysfunction.^{3,4}

Xylazine is an alpha-2 adrenergic receptor agonists,⁵ and it is most commonly used as a sedative agent in ruminants.⁶ Among all domestic animals, ruminants are the most sensitive to xylazine.⁷ The systemic administration of xylazine in ruminants is associated with moderate to severe cardiopulmonary depression such as bradycardia, hypotension, hypoxaemia and tachypnea.^{8,9,10} In recent years xylazine has been used epidurally to induce perineal analgesia in many species of animals such as horses,^{11,12} ponies,¹³ cattle,¹⁴ dogs,¹⁵ goats,^{7,16,17} sheep,⁹ buffaloes^{18,19} and llamas.²⁰ Combinations of xylazine and lidocaine have been shown to provide rapid onset and long duration of analgesia in horses²¹ and llamas.²⁰

Dromedary camels generally are found in tropical regions of the world and play a significant role in the socio-economic affairs of the nomadic people.^{22,23} Despite its significant contribution for human societies in tropical region, there have been very few systematic researches and expertise on camels.²³ Many of the principles of veterinary anesthesia, which are applied to the other species, will also apply to the camelids,²⁴ but it has been stated that camels may be susceptible to toxicity from some drugs at doses used commonly in other ruminants.¹ Some researches have been conducted to use of various analgesic agents for epidural anesthesia in South American camelids such as llamas and alpacas,^{20,25} but there are very few researches about utilization of epidural anesthesia in dromedary camels. Consequently, this study was performed to compare the effectiveness of analgesia following caudal epidural injection of lidocaine, xylazine, and a lidocaine/xylazine combination in dromedary camels.

Materials and Methods

A total of 15 immature dromedary camels 4 to 6 months of age of either sex, weighing 120-150 kg were selected for this study. The animals were housed in a pen and maintained on grass (hay) supplemented with concentrate. Drinkable water was made freely available. Camels were judged to be in good health based on clinical and haematological evaluations prior to the experiment. Food was withheld for 12 hours and water for 8 hours prior to the experiment. The trials were conducted in the morning hours of the day. During the course of the experiments the ambient temperature fluctuated between 25° and 27°C.

The animals were randomly assigned to three equal groups. In group L: lidocaine 2% (Pasteur Institute of Iran, Batch No: 86-347) 0.22 mg/kg; group X: xylazine 2% (Alfasan, Woerden-Holland, Batch No: 087238-3) 0.17 mg/kg and group LX: a combination of lidocaine and xylazine (0.22 and 0.17 mg/kg) was injected epidurally. The volumes of L and X injected were filled up with sterile saline solution so they equaled that of LX combination.

Before each treatment, the animals were restrained in sternal recumbency, and the skin over the sacrococcygeal area was prepared surgically. The injections were made into the epidural space through the first intercoccygeal space, using an 18 gauge 3.7 cm long hypodermic needle. The epidural space was confirmed by the hanging drop technique and lack of resistance to injection. Following drug injection, the camels were placed in standing position in a chute and observed for any drug-induced side effects. The observers were unaware of the drug dose administered at each study.

In the current study, analgesia was tested in the tail, anus, perineum and upper hindlimb using a pin prick method to determine the extent of complete analgesia following epidural administration of the drugs. Complete analgesia was defined as the lack of response to pin pricks. Existence or lack of response to pin pricks for each site was assessed during the study and compared between the groups subjectively.

The main focus of our study was on the onset time and duration of complete perineal analgesia. The period between the injection and loss of the sensation was considered as the onset time of complete analgesia.

Duration of the complete analgesia was determined by testing the response to stimulation of the skin of the perineum at time 0 (before injection), and 1, 3, 5, 10, 15, 20 minutes, then every five minutes until the end of complete analgesia by observing response to painful stimulation.

The ataxia was assessed by observing the hind limb position, swaying and leaning against the chute, and was recorded as ataxic or not ataxic. Sedation was scored on a four-point scale in each camel for each dose: 1 = alert (no sedative effect), 2 = mild sedation (reduced alertness with no other signs), 3 = moderate sedation (drowsiness and slight drop of head), 4 = deep sedation (marked drowsiness and drip of head).

Clinical parameters including heart rate (HR), respiratory rate (RR), and rectal temperature (RT) were assessed before drug administration and at 15 minutes intervals thereafter until 180 minutes.

Data analyses were performed by using SPSS software (SPSS 16.0, Chicago, IL, USA). The onset time and duration of ataxia and complete perineal analgesia were analyzed using one-way analysis of variance (ANOVA) followed by Post Hoc, Tukey HSD test for the comparison of mean \pm SD between the groups. Values for HR, RR and RT were analyzed by analysis of variance for repeated measures to determine if there were any differences between the groups during the 180 minute study. A paired sample t test was used to compare the mean at different time intervals with their base values within the group. A value of $p < 0.05$ was considered significant.

Results

Mild to moderate ataxia was observed in all test subjects following epidural administration of lidocaine, xylazine and their combination. The animals in group L and LX showed moderate ataxia, whereas mild ataxia was observed in group X.

Camels receiving the epidural xylazine or a combination of lidocaine and xylazine became mildly or moderately sedated, three animals in each group receiving sedation score of 2, and two animals, a score of 3. All five camels receiving epidural lidocaine were alert, reaching the sedation score of 1.

In each animal, loss of sensation to pin pricking was observed in the tail, anus, and perineum following epidural administration of lidocaine, xylazine and their combination. Hind limbs analgesia was not produced by either treatment. The onset time (minute) of complete perineal analgesia in group X (20.5 ± 3.32) was significantly longer than groups L (13.75 ± 3.5) and LX (11.75 ± 2.36) ($P < 0.05$); and there was no significant difference between group L and LX ($P > 0.05$). Duration (minute) of complete perineal analgesia in group LX (185.27 ± 12.24) was significantly longer than groups L (67.46 ± 6.27) and X (53.75 ± 8.54) ($P < 0.05$); and there was no significant difference between group L and X ($P > 0.05$) (Figure 1).

Significant changes from baseline values in group X were RT (decreased from 30-45 minutes), RR (decreased from 45-90 minutes), and HR (decreased from 45-75 minutes); and significant changes in group LX were RT (decreased at 30 minutes), RR (decreased from 45-105 minutes), and HR (decreased from 60-75 minutes). No significant changes from baseline values were observed in group L.

Differences in group L compared to groups X and LX were significant in relation to heart rate and respiratory rate changes over time (Table 1).

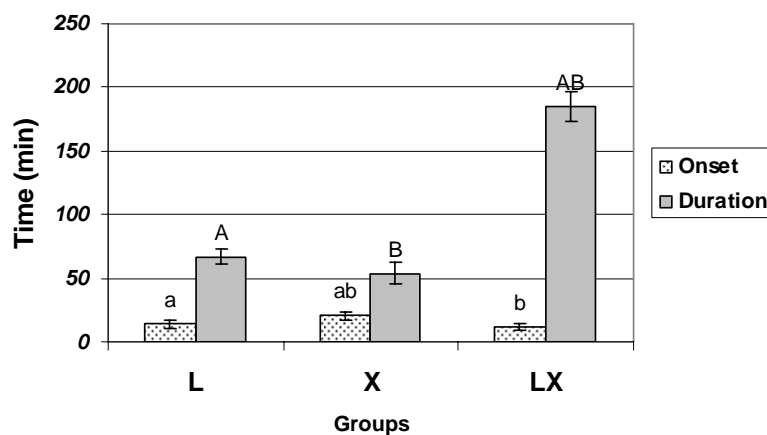


Figure 1- Mean \pm SD onset and duration of complete perineal analgesia following epidural administration of lidocaine (L), xylazine (X) and combination of xylazine and lidocaine in deromedaries. Same symbols shows significant difference between the groups ($P < 0.05$)

Discussion

Lidocaine is routinely used for caudal epidural analgesia in ruminants for a variety of obstetrical and surgical procedures, but large volumes can cause ataxia or even recumbency.²⁶ Lidocaine induced analgesia by inhibiting propagation and conduction of nerve impulses through blockade of sodium channels in the cells with subsequent prevention of depolarization.²⁷ The epidural analgesia induced by xylazine is mediated through α_2 -adrenoceptors in substantia gelatinosa of dorsal horn in spinal cord. There are high concentration of α_2 -adrenoreceptors in the dorsal horn of the spinal cord, where nociceptive fibers synaps, and also in the brainstem, where modulation of nociceptive signal is likely to be initiated. Analgesia produced by xylazine may be due to the inhibition of the release of substance P at level of substantia gelatinosa of the dorsal horn of the spinal cord.¹⁸ Co-administration of α_2 -agonists and local anaesthetics provides prolonged analgesia in human, horses, llamas, cows, buffalos and dogs.¹⁹

Table 1: Values of measured parameters (mean \pm SD) in dromedary camels before and following epidural administration of lidocaine (L), xylozine (X) and combination of lidocaine and xylozine (LX).

Time (min) Parameters	Baseline	15	30	45	60	75	90	105	120	150	180
HR (per min)											
L	51 \pm 3	50 \pm 2	50 \pm 1	50 \pm 3	48 \pm 2	48 \pm 3	50 \pm 2	49 \pm 2	50 \pm 3	50 \pm 2	50 \pm 1
X	52 \pm 5	48 \pm 4	45 \pm 2	43 \pm 2*	42 \pm 3*	43 \pm 4*	44 \pm 4	45 \pm 4	46 \pm 3	48 \pm 5	49 \pm 4
LX	55 \pm 5	48 \pm 5	46 \pm 6	45 \pm 5	44 \pm 4*	44 \pm 3*	46 \pm 4	47 \pm 5	48 \pm 5	48 \pm 4	48 \pm 3
RR (per min)											
L	14 \pm 2	13 \pm 2	13 \pm 2	13 \pm 2	13 \pm 1	13 \pm 2	13 \pm 2	12 \pm 2	13 \pm 1	13 \pm 1	13 \pm 2
X ^a	14 \pm 2	12 \pm 1	11 \pm 2	11 \pm 1*	11 \pm 1*	11 \pm 1*	11 \pm 1*	11 \pm 1	12 \pm 1	12 \pm 1	12 \pm 1
LX ^a	14 \pm 1	12 \pm 2	12 \pm 2	11 \pm 1*	11 \pm 1*	11 \pm 1*	11 \pm 1*	11 \pm 1*	11 \pm 3	11 \pm 2	11 \pm 2
RT (per 2min)											
L	37.35 \pm 0.19	37.32 \pm 0.24	37.32 \pm 0.21	37.30 \pm 0.14	37.35 \pm 0.24	37.33 \pm 0.22	37.30 \pm 0.21	37.35 \pm 0.19	37.37 \pm 0.26	37.38 \pm 0.19	37.34 \pm 0.22
X ^a	37.25 \pm 0.34	37.10 \pm 0.22	36.62 \pm 0.15*	36.77 \pm 0.22*	36.95 \pm 0.17	36.97 \pm 0.21	37.02 \pm 0.22	37.07 \pm 0.25	37.12 \pm 0.31	37.22 \pm 0.31	37.22 \pm 0.31
LX ^a	37.2 \pm 0.35	36.90 \pm 0.29	36.70 \pm 0.35*	36.82 \pm 0.35	36.82 \pm 0.34	36.77 \pm 0.32	36.85 \pm 0.40	36.92 \pm 0.38	37.00 \pm 0.35	37.00 \pm 0.36	37.05 \pm 0.37

HR: heart rate, RR: respiratory rate, and RT: rectal temperature

Symbol* shows significant differences compare to the baseline (p<0.05).

Symbol (a) shows significant difference with group L during the 180 minute study (p<0.05).

The additional effects of local anaesthetic agents and α_2 -agonists probably arise from several mechanisms. The exact mechanism by which α_2 -agonists induced prolongation of analgesia is not known.⁹ The possible mechanism of an α_2 -agonist induced prolongation of analgesia is through adrenoceptor mediated vasoconstrictors and inhibitions of local anesthetic vasodilatory effects and consequently delay subsequent vascular uptake.^{19,27} The prolongation of sensory blockade could also be explained by synergism between the antinociceptive effects of xylazine and the neural blocking action of lidocaine.²⁸ Alpha-2 agonists induced analgesia may intensify and prolong the lidocaine-induced sensory blockade through a pre or post-synaptic α_2 -mediated mechanism and/or an α_2 -agonist effect on arterioles^{19,27}.

The combination of xylazine and lidocaine was administered subarachnoidally to produce prolonged analgesia in goats. Despite the prolonged analgesia, using this combination is desirable for relieving postoperative pain.²⁹ The combination of lidocaine and xylazine administered epidurally to buffaloes produced an effective, safe, with more rapid onset of longer perineal analgesia, when compared with either agent alone.¹⁹ Epidural administered mixture xylazine/lidocaine was shown to induce safely prolonged analgesia in sheep and dairy cattle.^{9,30,31}

Injection of xylazine alone or in combination of lidocaine has been recommended in South American camelids (llamas).²⁴ Induction of caudal analgesia following epidural administration of lidocaine^{22,24} and ketamine³² has been stated in dromedaries. In recent years, the effects of epidural xylazine on clinical, hematological and biochemical parameters of dromedary camels has been investigated, but to the authors' best knowledge, there is no documented data about the administration of mixture of local anesthetic agents and α_2 -agonists for caudal epidural analgesia in this species. Grubb et al. (1993) evaluated the effects of epidural xylazine, lidocaine and their combination in llamas. They suggested that the onset of caudal analgesia was achieved in 3-4 min when using combination of xylazine (0.17 mg/kg) and lidocaine (0.22 mg/kg) or lidocaine alone. Epidural xylazine induced caudal analgesia within 20 min after injection. They reported co-administration of xylazine and lidocaine provides prolonged analgesia in llamas.²⁰

In agreement with other researchers who have worked on epidural analgesia in various ruminant species, the results of current study showed that epidural injection of combination of lidocaine and xylazine significantly prolonged duration of analgesia compared to the injection of lidocaine or xylazine alone. Also onset of analgesia following epidural injection of lidocaine and combination of lidocaine and xylazine was significantly shorter than injection of xylazine alone. It seems that epidural lidocaine is shorter act compared to the epidural xylazine.

Dose-related ataxia can be expected following epidural administration of lidocaine because it blocks both sensory and motor fibers.¹⁹ In the present study, moderate ataxia was seen after epidural injection of lidocaine and its combination with xylazine. Mild ataxia occurred after epidural xylazine alone and it is likely resulted from xylazine-mediated central sedative effects. Because of sedative effect of xylazine, the camels in group X and LX were moderately or deeply sedated, whereas the camels in group L were alert and nervous during the study. The xylazine injected in epidural space in groups X and LX that was subsequently absorbed systemically appeared to be sufficient to cause sedation in the dromedaries in the current study. There is a species-related variation in the sensitivity to α_2 -agonist. Some investigators feel that between ruminants species goats are more sensitive and South American camelids appear to be less sensitive to xylazine.³³ Horses do not generally become sedated after epidurally injected xylazine,²¹ although cattle³⁴ and llamas²⁰ may exhibit mild to moderate sedation. In the present study, it seems that dromedary sensitivity to epidural xylazine is same as llamas. Differences to response to epidural xylazine probably arises from species-related variation in the sensitivity to α_2 -agonist, concentration and total volume of the drug, injection sites and techniques, anatomical differences of spinal cord and spinal canal, and animal age.^{35,36}

In the present study, administration of epidural xylazine in the dromedaries of groups X and LX caused significant depression in HR, RR and RT values at different measurement points. Decreases in HR were reported after epidural injection of xylazine in cattle,¹⁴ sheep,³⁷ mares⁵ and goats.^{7,17} A significant drop in HR is considered a classical response following the administration of α_2 -adrenoceptor agonist.³⁸ The bradycardia recorded after the administration of xylazine could be attributed to decreased sympathetic outflow from CNS, 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 heart.³⁹

Similar results in depression of RR following injection of xylazine have also been reported in cattle,⁴⁰ horses⁴¹ and goats.⁴² All the α_2 -adrenoceptor agonists cause some degree of respiratory depression. This might be attributed to the direct depression of the respiratory centre through stimulation of supraspinal adrenoceptors following systemic absorption of the drug.¹⁸

A decrease in RT following systemic administration of α_2 -adrenoceptor agonists has been attributed to the depression of the hypothalamic thermoregulatory centre.⁴³ The decrease in RT was also probably to the result of reduced basal metabolic rate (BMR) and muscle activity, and depression of thermoregulatory centre.¹⁸

According to the results of present study the combination of lidocaine with xylazine (0.22 mg/kg and 0.17 mg/kg) produces comparable degrees of complete caudal 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 drugs 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 dromedaries.

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مقایسه اثر داروهای لیدوکائین، زایلازین و ترکیب لیدوکائین و زایلازین در بی حسی اپیدورال خلفی در شتر تک کوهانه

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هدف - مطالعه حاضر به منظور بررسی اثرات بی دردی ناشی از تزریق اپیدورال داروهای لیدوکائین، زایلازین و ترکیب آنها در شتر تک کوهانه انجام شد.

طرح مطالعه - مطالعه تجربی بر روی موجود زنده.

حیوانات - تعداد ۱۵ نفر شتر تک کوهانه نابالغ و سالم.

روش کار - در این مطالعه حیوانات بطور تصادفی به ۳ گروه مساوی تقسیم شدند. در گروه L: داروی لیدوکائین ۲٪ با دوز ۰/۲۲ میلیگرم به ازای کیلوگرم وزن بدن، در گروه X: داروی زایلازین ۲٪ با دوز ۰/۱۷ میلیگرم به ازای کیلوگرم وزن بدن و در گروه LX: ترکیب داروی لیدوکائین و زایلازین با دوزهای مذکور در اولین فضای بین مهره ای دم تزریق شد. زمان شروع و طول مدت بی دردی، شدت آرامبخشی و عدم تعادل و تعداد ضربان قلب و تنفس و درجه حرارت بدن قبل از تزریق و در فواصل زمانی معین بعد از تزریق اپیدورال داروهای مذکور ثبت گردید و بین گروهها مورد مقایسه گرفت.

نتایج - نتایج این بررسی نشان داد که تزریق اپیدورال داروهای لیدوکائین، زایلازین و ترکیب آنها سبب القای بی دردی در ناحیه دم، مقعد و پرینه گشت. زمان شروع بی دردی در ناحیه پرینه در گروههای L و LX بطور معنی داری کوتاهتر از گروه X و طول مدت بیدردی در گروههای X و LX بطور معنی داری طولانی تر از گروه L بود. آرامبخشی خفیف تا حد متوسط در گروههای X و LX مشاهده شد، در حلیکه حیوانات در گروه L در طول مطالعه هوشیار و عصبی بودند. عدم تعادل متعاقب تزریق اپیدورال دارو در تمام حیوانات مشاهده شد که در L و LX شدیدتر بود. تضعیف معنی داری در تعداد ضربان قلب و تنفس و درجه حرارت بدن در بعضی از زمانهای بعد از تزریق دارو در گروههای X و LX ثبت شد.

نتیجه گیری و کاربرد بالینی - بر پایه نتایج حاصله میتوان اینگونه نتیجه گیری نمود که تزریق اپیدورال ترکیب داروهای لیدوکائین و زایلازین سبب القای بی دردی خلفی موثر، امن با شروع اثر سریع و طولانی مدت نسبت به تزریق تنهای داروهای مذکور در شتر تک کوهانه میگردد.

کلید واژگان - اپیدورال، لیدوکائین، زایلازین، شتر تک کوهانه.

