IJVS 2014; 9(2); Serial No:21

IRANIAN JOURNAL OF VETERINARY SURGERY (IJVS)
WWW.IVSA.IR

Caudal Epidural Analgesia Using Lidocaine Alone and in Combination with Tramadol in Dromedary Camels

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Abstract

Objective- This study was performed to investigate the analgesic effects of lidocaine and lidocaine/tramadol combination in epidural anaesthesia in dromedary camels**.**
Design- Experimental Study
Animals- Eight healthy immature dromedary camels
Procedures- The camels were randomly designed in 2 equal groups. In group L: lidocaine 2% (0.22 mg/kg) and in group LT: a combination of lidocaine 2% (0.22 mg/kg) and tramadol (1 mg/kg) were injected into the first inter-coccygeal (Co1–Co2) epidural space. Onset time and duration of caudal analgesia, sedation and ataxia levels were recorded after drug administration.
Results- Epidural lidocaine and co-administration of lidocaine and tramadol produced complete analgesia in the tail, anus and perineum. There were no significant differences in onset and duration of caudal analgesia parameters between groups L and LT ($p>0.05$). Epidural administration of the lidocaine–tramadol combination resulted in mild to moderate sedation, whilst the animals that received epidural lidocaine alone were alert and nervous during the study. Ataxia was observed in all test subjects and was slightly more severe in camels that received the lidocaine–tramadol mixture.
Conclusion and Clinical Relevance- It was concluded that epidural administration of lidocaine plus tramadol resulted in sedation and unnoticeable longer caudal analgesia in standing conscious dromedary camels compared with the effect of administering lidocaine alone.
Key Words- Epidural, Lidocaine, Tramadol, Dromedary camels.

Introduction

Ruminants are generally not considered to be good subjects for general anaesthesia, mainly because of hazards of regurgitation and inhalation of ruminal contents or saliva into the lungs if the airway is left unprotected. Thus, regional anesthesia produced by the perineural or epidural injection of anesthetic agents is most frequently employed in these species. Caudal epidural analgesia can be used to perform surgery of the perineum, rectum, and vagina in standing animals and most commonly produced by local anesthetics (usually lidocaine 2% solution) injected into the caudal epidural space.[1] Lidocaine is routinely used for caudal epidural analgesia in ruminants, but large volumes can cause ataxia or even recumbency. To facilitate reproductive manipulations, the onset of analgesia should be faster and shorter and should not interfere with the motor system.[2] 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.[3] Epidural 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 by highly selective actions on spinal receptors which selectively block sensory fibers, thereby providing significant analgesia with decreased likelihood of rear limb dysfunction.[4,5]
Tramadol, a synthetic racemic mixture of the 4-phenyl-piperidine analogue of codeine, has received widespread acceptance in human medicine since it was first introduced in 1977 in Germany.[6,7] Its efficacy is attributed to a dual mechanism of action, namely, the interaction with opioid μ receptors and the monoaminergic effect on spinal pain modulation

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through inhibition of the reuptake of norepinephrine and serotonin. Its affinity for opioid μ receptors is approximately 10 times less than codeine and 6000 times less than morphine. Recently, it has been shown that tramadol has local anesthetic action either by producing analgesia after intradermal injection ,[8,9] or by reducing pain associated with propofol administration.[10,11] The pharmacological profile of tramadol such as activation of opioid receptors, inhibition of the monoaminergic system and local anesthetic effects,[12,13,9] makes it an attractive drug for epidural administration. Epidural administration of tramadol alone or in combination with lidocaine or other sedative agents has been reported to produce perineal analgesia in a number of ruminant species and other species, for example cattle,[14] lamb,[15] goats[16] dog,[17] and horse.[18]

Approximately 90% of the world's camels are dromedaries [19] which play a significant role in the socio-economic affairs of nomadic people in providing meat, milk and wool. They are also used for transportation.[19, 20] Many of the principles of veterinary anaesthesia that apply to other ruminant species also apply to the camelids,[21] But camels may be susceptible to toxicity from some drugs at doses used commonly in other ruminants.[1] There are currently only a few published studies about epidural analgesia in camels. In recent years, clinicophysiological effects of epidural administration of various sedative agents have been investigated in dromedaries. Epidural administration of lidocaine, xylazine,[22, 23] ketamine,[24, 25] medetomidine[26] alone or in combination have been investigated in dromedary camels, but to the authors' knowledge, there are no documented data about epidural co-administration of lidocaine and tramadol in dromedary camels. The purpose of the present study was to serve as a preliminary investigation of epidural administration of lidocaine and a combination of lidocaine and tramadol in dromedaries.

Materials and methods

Eight immature male dromedary camels (8–12 months of age), weighing 200 kg – 220 kg, were used in this study. The animals were housed in a pen, fed grass (hay) supplemented with concentrate and drinkable water was made freely available. Camels were judged to be in good health based on clinical evaluation. Food was withheld for 24 h and water for 12 h prior to the experiment. The animals were randomly assigned to one of two groups. In group L, 0.22 mg/kg lidocaine 2% (Shahid Ghazi Pharmaceutical Co. Tabriz, Iran) was injected epidurally, whilst in group LT, a combination of 0.22 mg/kg lidocaine 2% and 1 mg/kg tramadol (50 mg/ 1ml, Tehran Chemie, Iran) was injected epidurally. Before each treatment, the animals were restrained in sternal recumbency and the skin over the sacrococcygeal area was prepared surgically. The injections were administered into the extradural space through the first intercoccygeal (Co1–Co2) 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 walked into a chute and observed for any drug-induced side-effects. In this study, analgesia was tested in the tail, anus, perineum and upper hind limb using a pinprick method. This constituted the insertion of a 23-gauge needle through the skin into the underlying tissues at the tail base, anus, perineum and upper hind limb area. 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, leaning against the chute and swaying, and was recorded as ataxic or not ataxic.

Data analyses were performed using SPSS software (SPSS 16.0, Chicago). The mean ± standard error of onset time and duration of complete perineal analgesia were analyzed using the Student t test to compare the data between the two groups. A value of $p \leq 0.05$ was considered significant. Ataxia and sedation levels were compared between the groups, descriptively.

Results

In our clinical finding, mild (rear limb abduction) to moderate ataxia (swaying) was observed in all animals of both groups during the experiment. The animals in group LT showed a little more ataxic signs compared to the group L, but recumbency did not occur in any of the animals. The camels receiving epidural lidocaine were alert and nervous during the study, but mild to moderate sedation symptoms such as reduced alertness, drowsiness and slight drop of head were observed in the animals receiving epidural lidocaine-tramadol mixture.

In each animal, loss of sensation to pin pricking was observed in the tail, anus, and perineum following epidural administration of lidocaine and lidocaine-tramadol combination. Hind limbs analgesia was not produced by either treatment. Data analysis showed that there was no significant difference in the onset time (minute) of complete perineal analgesia between groups LT (9.25±1.25) and L (12.5±1.89) (P>0.05). The results of present study also showed although the duration of

complete perineal analgesia in group LT (61±4.27) was longer than group L (55±5.4), but the difference was not significant (P>0.05) (Fig 1).

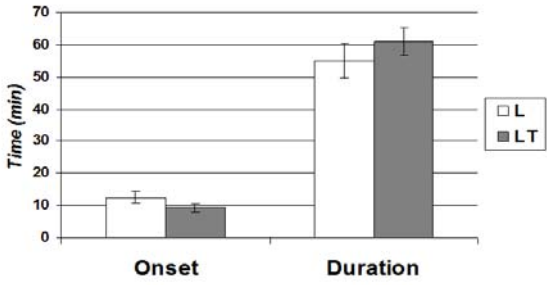

Figure 1- Mean ± SE onset and duration of complete perineal analgesia following epidural administration of lidocaine (L) and combination of lidocaine and tramadol (LT) in deromedaries.

Discussion

Lidocaine is one of the most common drugs used for epidural caudal analgesia in animals.[2] Analgesia provided by lidocaine is relatively short duration and may require re-administration of the agent, which can cause unwanted effects including recumbency.[2] Recently, researchers have focused on epidural administration of other drugs such as α2 agonists, opioids and anesthetic agents solely or in combination, to accelerate the onset of caudal analgesia, prolong the duration of analgesia and reduce the incidence of adverse effects.[27]

Epidural opioid administration is one of the most common techniques for postoperative pain control. Epidural administration of low-dose opioids induces strong and long-lasting segmental analgesia via opioid receptors.[28] However, the known adverse effects of epidural opioids require a very careful selection of the agent and dosage.

Tramadol is a weak agonist at all types of opioid receptors with some selectivity for μ-receptors. Also, tramadol inhibits the reuptake of norepinephrine and serotonin, thus increasing the concentrations of these two neurotransmitters in the central nervous system. The pharmacological profile of tramadol such as inhibition of the monoaminergic system, activation of opioid receptors, and local anesthetic effects[12,13,9] makes it an absorbing drug for epidural administration.

Many studies have investigated the efficacy of caudal analgesia following caudal epidural injection of tramadol in horses,[18,29] dogs [17,30,31] and different species of ruminants including cattles[14,32] and goat.[16] The present study is the first to investigate the comparison effect of lidocaine with tramadol-lidocaine combination given by epidural injection to camels. The dose of tramadol chosen in the current study (1 mg/kg) was based on epidural used doses of tramadol in ruminant and horse in the veterinary literature and pervious researchs.[14,15,16,33] The results of the present study revealed that the combination of tramadol at a dose of 1 mg/kg with lidocaine induced sedation in comparison with epidural lidocaine alone. The results showed no significant differences were observed in the onset time and duration of caudal analgesia between the two groups, although analgesia period has unnoticeably prolonged in group LT compared to the group L.

In two individual studies, Habibian et al. (2010 & 2012) evaluated caudal analgesic effects following epidural co-administration of tramadol and lidocaine in lamb and goat. They stated that a mixture of tramadol and lidocaine provided a longer duration of analgesia compared to lidocaine as a sole agent in both species.[15,16] It has been reported that the duration of analgesia in cows following epidural co-administration of tramadol and lidocaine was longer in comparison with lidocaine, solely; while there were no significant differences in the onset of analgesia.[14] In the present study, animals of both groups showed varied signs of ataxia. The camels in group LT were more ataxic and it is more likely resulted from tramadol-mediated central sedative effects. Because of sedative effects of tramadol, the camels in group LT were mildly or moderately sedated, whereas the camels in group L were alert and nervous during the study. Despite of the previous studies which have pointed out the epidural administration of combination of lidocaine-tramadol significantly prolong the caudal analgesia period in ruminants, the results of our study show that the mentioned combination has no significant effects on duration of caudal analgesia in comparison with lidocaine alone in camels. Differences to response to epidural analgesic agents probably arises from species-related variation in the sensitivity to drugs, concentration and total volume of the drug, injection sites and techniques, anatomical differences of spinal cord and spinal canal, and animal age.[34,35]

According to the results of this study, although epidural administration of a combination of tramadol (1 mg/kg) and lidocaine (0.22 mg/kg) did not enhance significantly the caudal analgesia or speed up the onset of analgesia compared with lidocaine alone, but this combination could induce mild to moderate sedation in camels, therefore may allow veterinarians to perform related clinical procedures with more comfort and less stress. Further research is needed to study the mechanism of interaction of lidocaine and tramadol at the spinal cord level and dose optimization between lidocaine and tramadol in dromedaries.

Acknowledgments

This work was supported financially by a Grant for Scientific Research from Vice Chancellor of Research of Shahid Bahonar University of Kerman, Iran.

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نشریه جراحی دامپزشکی ایران
سال ۲۰۱۴، جلد ۹ (شماره ۲)، شماره پیاپی ۲۱

چکیده

بی‌حسی اپیدورال خلفی متعاقب تزریق تنهای داروهای لیدوکایین و ترکیب آن با ترامادول در شتر تک‌کوهانه

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هدف- مطالعه حاضر به منظور بررسی اثرات ب دردی ناشی از تزریق اپیدورال داروهای لیدوکایین و ترکیب ن با ترامادول در شتر تک-کوهانه انجام شد.

طرح مطالعه- مطالعه تجربی بر روی موجود زنده.

حیوانات- تعداد ۸ نفر شتر تک‌کوهانه نابالغ و سالم.

روش کار- در این مطالعه حیوانات بطور تصادفی به۲ گروه مساوی تقسیم شدند. در گروه L: لیدوکایین با دوز ۰/۲۲ میلیگرم به ازای کیلوگرم وزن بدن و در گروه LT ترکیب داروهای ترامادول با دوز ۱ میلی‌گرم به ازای کیلوگرم وزن بدن و لیدوکایین با دوز مذکور، در اولین فضای بین مهره‌ای دم تزریق شد. زمان شروع و طول مدت بی‌دردی، شدت آرام‌بخشی و عدم تعادل بعد از تزریق اپیدورال داروهای مذکور ثبت گردید و بین گروه‌ها مورد مقایسه گرفت.

نتایج- نتایج این بررسی نشان داد که تزریق اپیدورال داروهای لیدوکایین و ترکیب آن با ترامادول سبب القای بی‌دردی در ناحیه دم، مقعد و پرینه گردید. ارزیابی داده‌ها نشان داد که زمان شروع بی‌دردی و طول مدت آن بین دو گروه مورد مطالعه تفاوت معنی‌داری نداشتند ($P>0.05$). در طول دوره مطالعه آرامبخشی خفیف تا حد متوسط در گروه LT دیده شد، اما در گروه L حیوانات کاملا" هوشیار و عصبی بودند. علائم عدم تعادل متعاقب تزریق اپیدورال دارو در تمام حیوانات گروههای L و LT مشاهده شد، در حالیکه عدم تعادل در حیوانات گروه LT شدیدتر بود.

نتیجه‌گیری و کاربرد بالینی- بر پایه نتایج حاصله میتوان اینگونه نتیجه‌گیری نمود که تزریق اپیدورال ترکیب داروهای لیدوکایین و تراماول سبب افزایش معنی‌دار در طول مدت بی‌دردی خلفی نسبت به تزریق تنهای لیدوکایین نگردید، اگرچه ترکیب فوق سبب ایجاد علائم آرام‌بخشی در شتر تک‌کوهانه می‌گردد.

کلمات کلیدی- اپیدورال، لیدوکایین، ترامادول، شتر تک‌کوهانه.