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Epidural Xylazine Reduced Ketamine Anesthetic Requirements in Laparoscopic Ovariohysterectomy in the Dog

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Abstract

Objectives: To evaluate if epidural administration of xylazine could decrease the effective dose of intravenous ketamine for maintenance of general anesthesia in laparoscopic procedures and assessment of related complications during anesthesia.
Design: Experimental Study.
Animals: 20 Female dogs with 21.0 ± 3.0 kg weight and 18.0 ± 1.2 months age.
Material and methods: Animals randomly divided into two groups (n=10). All dogs premedicated with acepromazine. Anesthesia induced by combination of ketamine and diazepam. In one group xylazine injected epidurally then all of them spayed by same laparoscopic method and repeated doses of ketamine for maintenance of anesthesia. Cardiopulmonary parameters such as SpO_2 and $ETCO_2$ during operation were recorded.
Results: There were no significant differences in weight and age between two groups. Mean of ketamine administration in group 1 was 640 mg and in group 2 (have epidural administration of xylazine) was 270 mg.

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Conclusions and Clinical Relevance: Data analysis showed that epidural administration of xylazine, decreases the amount of ketamine needed to maintain anesthesia ($P<0.05$) with no significant difference in cardio-pulmonary parameters during laparoscopic operation. Epidural injection of Xylazine could be used as a concurrent medication in general anesthesia without complication. Analgesic effects of xylazine decreased the use of ketamine ($P<0.05$) by repeated dose based on intra operative pain reflex during anesthesia.
Key words: Epidural anesthesia, laparoscopy, dog.

Introduction

The mechanism of action of alpha-2 receptors is mainly through their agonist activity at presynaptic alpha-2 adrenergic receptors that results in decrease in release of norepinephrine from adrenergic nerve terminals in CNS and periphery. This causes sedation, decreased sympathetic activity, analgesia, and hypotension.[1] Among the alpha-2 agonists, medetomidine and xylazine are the most commonly used in small animal practice [1]. Their cardiovascular effects include, initial transient hypertension followed by prolonged hypotension (biphasic changes), bradycardia, second degree atrioventricular block, and decreased cardiac output, [1, 2] and their respiratory effects include decreased respiratory rate, with a variable effect on tidal volume (at clinically practical dose it is of minor concern).[1] Other effects of this groups that may have clinical importance are: increasing blood glucose level, decreasing intestinal motility, increasing urine production, increasing uterine contractions which may lead to premature delivery or abortion, and inducing of vomiting.[3] One of the main benefits of using alpha-2 agonists is to decrease the induction dose of anesthetic agents to reduce their side effects. Today, using of these agents during and post anesthetic period became popular to control complications during anesthesia and improve quality of recovery.[1, 4] Routes of administration for alpha-2 agonists had been studied in many researches. Epidural administration were used first in dairy cattle with combination of lidocaine and then tried with other drugs in horses.[5, 6, 7] Epidural anesthesia in other animals was not approved as a sole method for painful surgical operation, but it is used as a concurrent method for pain management especially in combination with those anesthetic agents which has less analgesic activity.[8, 7] It has been shown that epidural administration of xylazine has sparing action on isoflurane anesthetic requirements.[9]

In small animal practice, the intravenous and inhalation anesthesia is the commonest methods for intra and postoperative analgesia. The preoperative alleviation of pain is entirely depends on analgesic properties of premedication drugs and intravenous and inhalation agents, used for premedication and maintenance of the anesthesia.[2, 10]

Generally, these methods provide a minimal postoperative analgesia. The epidural administration of local anesthetic drugs with opioids or alpha2-adrenergic agonists provide an excellent intra- and post-operative analgesia.[3, 4]The main purpose of this evaluation is to determine the effects of epidural xylazine on quality of anesthesia during laparoscopic method for ovariohysterectomy in dogs.

Material and Methods

Twenty female mixed breed dogs were chosen and prepared for an experimental procedure. The average of weight was 21.0 ± 3.0 kg and the average of age was recorded 18.0 ± 1.2 months .Clinical and blood biochemical examinations before operation did not show any sign

of diseases or disturbances. All experiments were performed according to European Animal Care Committee guidelines. Dogs spayed by laparoscopic method as elective procedures with no technical complications. They randomly divided into two groups (n=10). In all dogs acepromazine (KELA Laboratoria NV. Hoostraten/Belgium) (0.05 mg/kg) administrated by intramuscular route as premedication. Induction of anesthesia accomplished by intravenous injection of ketamine (10 mg/kg) (alfasan. Woerden-Holland) and Diazepam (Dr. Amidi Ins. Iran) (0.2 mg/kg). For maintenance of anesthesia repeated injection of ketamine (5 mg/kg) where used following sudden increase in heart and respiratory rates and pattern during anesthesia. In group two injection of xylazine (alfasan. Woerden-Holland) (0.25 mg/kg) in epidural space after induction of anesthesia was performed. The area above the epidural space was shaved and aseptically prepared with povidone-iodine 10%. The lumbosacral interspace was identified through iliac crests and the processes of last lumbar (L7) and the first sacral (S1) vertebra. It was palpated in both directions (cranially and caudally) moving the fingers over the spinous processes of L6-L7 and S1-S2. The needle (20 gauge, 3.8 cm length) was inserted perpendicularly to the skin in the deepest place (in the middle between L7 and S1) between both spinous processes. All epidural injections were performed by an experienced anesthesiologist. Placement of the spinal needle was confirmed by a loss of resistance to injection of air or saline, lack of aspirate from the needle and lack of resistance to injection.

In group one the same amount of normal saline was administered epidurally. At the end of the operation the whole amount of ketamine that administered during the operation was determined.

All animals were treated post operatively with cefazoline (25mg/kg-every 8 hours-5 days-IM) and ketoprofen (2 mg/kg, IV, q12h).

Amount of ketamine used for each group prior and during the surgical intervention, was calculated.

The following parameters were monitored: temperature, heart rate, respiratory rate, saturation of hemoglobin oxygen and end tidal carbon dioxide. The recording of these parameters accomplished by a pulseoxymeter (Envitec-Germany) and a capnometer (Envitec- Germany), in all dogs, every 10 minutes from 10 minutes before beginning the operation till complete recovery from anesthesia.

Data were compared between epidural and nonepidural treatments. Significant difference was observed with one-way analysis of variance using SPSS (SPSS Inc., Chicago, IL, USA).

Results

Ten mg/kg ketamine was administered i.v. for induction of anesthesia in all dogs. In group one which had no epidural xylazine administration, the repeated ketamine injection for maintenance of anesthesia showed larger volume in comparison with group two (640 mg versus 270 mg). The statistical analysis showed significance of this difference ($P = 0.012$) (Fig. 1). At time points no significant differences over time were observed between the two groups in heart rate evaluation, also in respiratory rate there were no significant differences ($P > 0.05$).

Results of end tidal CO_2 measurements did not show sever hypoventilation during anesthesia in both groups. Comparison of these data between groups also did not show any significant difference ($P > 0.05$) (Fig. 2).

Mean of hemoglobin saturation measurements in two groups did not show any significant difference ($P > 0.05$). But in specific time intervals, statistical comparisons detected a

significant decrease in hemoglobin saturation in group two at 40 minute point after induction which did not extended more during anesthesia (P=0.028) (Fig. 3).

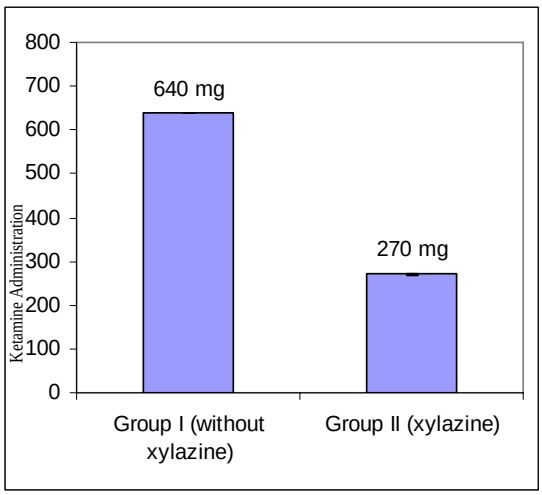

Figure 1. Mean of ketamine administration (mg) in two groups

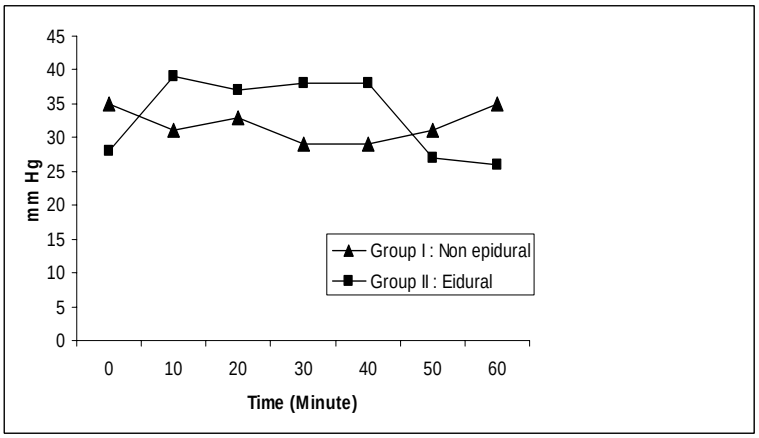

Figure 2. Mean of End tidal carbon dioxide in two groups during anesthesia

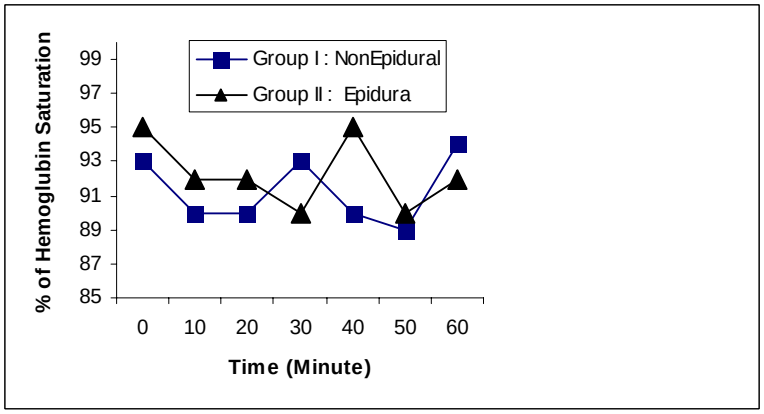

Figure 3. Mean of oxyhemoglubin saturation in two groups during anesthesia

Discussion

Epidural injection of alpha 2-adrenergic agonists have a comprehensive history in large animal medicine , especially in dairy cattle and mare as a sole method or in combination with other analgesic or local anesthetic agents.[11, 8, 7] Combination of alpha2-adrenergic agonists with opioids to extension of analgesic effect with concurrent sedation where considered in small animal pain management as well as other combination of opioids and alpha2-adrenergic for moderate anesthetic combination protocol e.g., neuroleptic analgesia.[5, 12] Many researches on laboratory animals indicate that the epidural co-administration of alpha 2-adrenergic agonists and an opioid would be effective for experimentally pain management due to mimic the effect of descending antinociceptivefibers originating in the spinal cord which utilize norepinephrine as a terminal neurotransmitter, thus providing a potential binding site for the alpha2-adrenergic agonists.[2, 4]

This antinociceptive mechanism results in inhibition of the rostral transmission of nociceptive impulses at synapses between peripheral fibers and ascending fibers in the dorsal horns by hyperpolarization of presynaptic membranes and inhibition of neurotransmitter release [13] as well as via postsynaptic inhibition of rostral transmission. [4]

Intravenous anesthesia using repeated injection of ketamine is an old version of continues infusion of ketamine which is used in animal laboratory research centers for short time procedures in substitution of inhalation and total intravenous anesthesia facilities to decrease time and equipment due to common economic problems.[3, 1] In this method, combination of ketamine and diazepam provide a rapid and smooth induction and the repeated injection of ketamine for maintenance of anesthesia is depended on the response of dogs to surgical stimulation.[3, 10, 14] Since somatic analgesic effect of ketamine is poor and does not provide good visceral analgesia, it is necessary to use in combination with an analgesic agent. However this problem could be solved by premedication by opioid premedication or an alph2 agonist, but using epidural anesthetic method could control side effect of short term dissociative agents for such these procedures.[2, 3, 1]

In abdominal cavity or laparoscopic operation which visceral analgesia is important, when ketamine is used for short term surgeries, epidural anesthesia is useful for pain management and decrease in ketamine side effects.[5, 1, 14] The epidural administration of xylazine in combination with i.v. administration of ketamine was experimentally used for general anesthesia in this study. As results determined, the epidural injection of xylazine could decrease intravenous repeated dose of ketamine due to antinociceptive mechanism of xylazine and it may contributed to the analgesic effect of epidural administration of xylazine which was detected in several past studies.[2, 6, 4] It was determined that use of xylazine as an intramuscular premedication make a mild analgesic effect and could decrease the ketamine volume for induction of anesthesia.[5, 1] Also similar researches published about other alpha 2 agonists which could decrease maintenance dose of propofol during anesthesia and even could be effective on minimum alveolar concentration of inhalation anesthetic such as halothane.[2, 1, 15] A similar study about combination of epidural xylazine and intravenous propofol showed that, xylazine not only can alleviate propofol volume , but also could make better recovery and lessens extubation time , which was not evaluated in our study. [15]

Although intramuscular and intravenous administration of xylazine causes bradycardia but no significant decrease in heart rate detected in this study. It would be contributed to sympathomimetic effects of ketamine that induce tachycardia and overlap with xylazine effects on heart rate. Also any significant difference between respiratory rate in two groups was not detected. Because ketamine increase respiratory rate and tidal volume in dogs, but

xylazine make a mild depression in respiratory rate which was not seen in this study. Changes in hemoglobin saturation were the same at minute 40 of anesthesia between groups which was predictable because of the same anesthetic conditions and surgical procedures. End Tidal carbon dioxide measurement is an important parameter in anesthesia monitoring of laparoscopic procedures which carbon dioxide gas used for insufflations of abdominal cavity. In this study significant differences did not observed between groups and no sever hypoventilation detected.

In conclusion according to data analysis of this study, use of epidural xylazine did not make critical cardiopulmonary effects during induction and maintenance of anesthesia with ketamine and minimized the ketamine side effect by decreasing its dose.

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چکیده:

اثر تجویز اپی‌دورال زایلازین بر کاهش کتامین مورد نیاز بیهوشی در برداشت رحم و تخمدان به روش لاپاروسکوپی در سگ

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هدف- این مطالعه به منظور بررسی اثر تجویز اپی دورال زایلازین بر میزان کتامین وریدی مورد نیاز برای بیهوشی عمومی در جراحی های لاپاروسکوپیک و ارزیابی پیچیدگی های احتمالی حین عمل، به انجام رسید.

نوع مطالعه- مطالعه تجربی.

حیوان مورد مطالعه- ۲۰ سگ ماده با وزن۳±۲۱ کیلوگرم و سن ۱/۲±۱۸ ماه.

مواد و روش کار- حیوانات بطور تصادفی به دو گروه ۱۰ تایی تقسیم شدند. به عنوان داروی پیش بیهوشی اسپرومازین به حیونات تجویز شد. سپس القا بیهوشی با تجویز کتامین به همراه دیازپام به انجام رسید. در یک گروه زایلازین بصورت اپیدورال تجویز شد. سپس در تمام حیوانات عمل برداشت رحم و تخمدان ها با یک روش لاپاروسکوپیک یکسان صورت پذیرفت. برای نگهداشتن بیهوشی از تکرار تجویز کتامین استفاده شد. رفلکس ها ی پلکی و قرنیه ای و پارامترهای قلبی-تنفسی مانند اشباع هموگلوبین از اکسیژن (SpO_2) و $ETCO_2$ در طی جراحی ثبت شدند.

نتایج- سگ های مورد استفاده در این مطالعه تفاوت معنی داری از نظر وزن وسن نداشتند. متوسط مصرف کتامین در سگ های گروه ۱ در مجموع ۶۴۰ میلی گرم بود و در سگ های گروه ۲ (گروهی که در آنها تجویز اپی دورال زایلازین انجام می شد) ۲۷۰ میلی گرم.

نتیجه گیری- تحلیل داده ها نشان داد که تجویز زایلازین میزان کتامین مورد نیاز برای نگهداری بیهوشی را در سگ های مورد مطالعه کاهش می دهد، بدون اینکه اثر معنی داری بر پارامترهای قلبی-تنفسی داشته باشد. می توان از تجویز همزمان اپی دورال زایلازین با بیهوش کننده های عمومی برای کاهش میزان داروی بیهوش کننده عمومی مورد نیاز بدون ایجاد پیچیدگی خاصی استفاده کرد. اثرات بی درد کننده زایلازین می تواند میزان نیاز به کتامین را در طی بیهوشی عمومی کاهش دهد.

لغات کلیدی- بی حسی اپی دورال، لاپاروسکوپی، سگ.