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Effect of Epidural Anesthesia with Lidocaine and Bupivacaine on Gastrointestinal Transit Time in Healthy Dogs

Hadi Imani[*1], Abdolvahed Moarabi[1], Ali Baniadam[1], Ahmad Khajeh[2], Fereshteh Alipour[3]

Abstract

Objective- To evaluate the effect of epidural anesthesia with lidocaine and bupivacaine on transit time of barium sulfate contrast medium through gastrointestinal (GI) tracts in healthy dogs.
Design- Prospective, randomized experimental study.
Animals-Five healthy mixed breed male dogs with 19.2±7.8 months age and 19.9±3.3 kg weight
Procedure- The animals received one of the treatments of saline (SAL), lidocaine (LID; 4 mg/kg; 20 mg/mL), and bupivacaine (BUP; 1 mg/kg; 5 mg/mL) in epidural space, randomly. The total volume of all injections was adjusted with normal saline to 0.22 mL/kg. All the dogs received the three treatments with at least one week interval. After oral administration of barium sulfate (3 mL/kg), serial left lateral radiographs were taken at 0, 20, 40, and 60 minutes and then every one hour till reaching the contrast medium to the colon. Thereafter, radiographs were obtained every 24 hours until the full evacuation of the contrast medium from the GI tract was seen.
Results- The time to the onset of gastric emptying was significantly lower in LID and BUP compared to SAL ($p<0.05$). The time to the completion of gastric emptying, reaching the contrast medium to the colon, and full evacuation of the contrast medium from the GI were not significantly different among groups ($p>0.05$).
Conclusion and Clinical Relevance- Epidural anesthesia with lidocaine and bupivacaine could reduce the onset of gastric emptying of barium sulfate contrast medium in healthy dogs.
Key Words- Epidural, Lidocaine, Bupivacaine, Transit time, Dog.

Introduction

Epidural anesthesia/analgesia is frequently used in dogs mostly for surgeries in hind limbs. This technique could also be employed to control or to reduce pain in peri-anal and peri-vulvar surgeries, orchiectomy and cesarean section in dogs.[1] Epidural anesthesia has several advantages over general anesthesia such as lowering the risk of general anesthesia with lesser hemodynamic changes produced by this technique. Epidural anesthesia could also be used concomitant with general anesthesia for management of perioperative pain.[2]

[1]Department of Veterinary Clinical Science, Faculty of Veterinary Medicine, Shahid Chamran University of Ahvaz, Ahvaz, Iran.
[2]Resident in Veterinary Surgery, Department of Clinical Science, Faculty of Veterinary Medicine, Shahid Chamran University of Ahvaz, Ahvaz, Iran.
[3]Student of Veterinary Medicine, Faculty of Veterinary Medicine, Shahid Chamran University of Ahvaz, Ahvaz, Iran.
Address all correspondence to Dr. Hadi Imani (DVM, DVSc).
E-mail: h.imani@scu.ac.ir
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However epidural anesthesia could be achieved by different classes of drugs, it is mostly provided by local anesthetics. Among local anesthetics, lidocaine and bupivacaine are the two most agents employed for epidural anesthesia/analgesia in dogs. Lidocaine and bupivacaine are belonging to the amino-amid group of local anesthetics which could provide short and long duration of anesthesia, respectively.[3]
Epidural application of local anesthetics has been suggested that could affect gastrointestinal (GI) motility;[4] However, this effect is in controversy.[4,5] Postoperative epidural anesthesia/analgesia with local anesthetics has been associated with earlier defecation and flatus in humans undergone major abdominal surgeries.[4,6,7] In addition, epidural bupivacaine has increased intestinal blood flow during colorectal surgery in human patients.[8] In contrast, several studies were not able to show any differences in GI motility following epidural anesthesia with local anesthetics in various types of abdominal surgeries in humans.[9-12] One study by Jansen et al. (2002) showed that postoperative epidural anesthesia with bupivacaine could lessen

intestinal paralysis in dogs which a short segment of colon resected.[5]

To the best of the authors` knowledge, most studies evaluated the effects of epidural anesthesia have been performed in patients with abdominal surgeries and no study has yet assessed the effects of epidural local anesthetics on GI motility in healthy subjects. Therefore, the objective of the present study was to evaluate the effect of epidural application of lidocaine and bupivacaine on transit time of barium sulfate contrast medium through the GI tract of healthy dogs.

Materials and Methods

The protocol of the present study was approved by Institutional Animal Care and Research Committee of the Faculty of Veterinary Medicine, Shahid Chamran University of Ahvaz, Iran. Five healthy mixed breed male dogs with mean±SD of 19.2±7.8 months age and 19.9±3.3 kg weight were used. The dogs were transferred to the hospital of Faculty of Veterinary Medicine at least two weeks before the beginning of the study. Health status was established by a thorough physical examination, complete blood count (CBC) and total protein (TP) measurement. The dogs were limited in separate cages with receiving feed (chickens` head and foot) twice a day and water *ad libitum*. Fasting and water limitation were done for the each dog about 18 and two hours before the experiments, respectively.

On the day of examination, the dogs were transferred to the place of the study. Thirty minutes was allowed to the dogs to be acclimatized to the environment. Then, ketamine (5 mg/kg; Rotexmedica, Trittau, Germany) and acepromazine (0.05 mg/kg; Alfasan. Wperden. Holland), combined into a single syringe, was administered into the hamstring muscles of the left thigh. Fifteen minutes later, the dogs were transferred on table and restrained in sternal recumbency. Epidural area was identified, clipped and aseptically prepared. The technique used for epidural anesthesia in the present study was the same of Valverde (2008).[2] In brief, a 20G needle was introduced perpendicular to the skin into the lumbosacral space until the tip of the needle encountered to the floor of the epidural space. Then the needle was withdrawn 1-2 mm. Ensuring the correct placement of the needle in the epidural space was performed by hanging drop test. After certainty of the correct site of the needle, one of the three treatments of saline (SAL), lidocaine (LID; 4 mg/kg; 20 mg/mL; Aburaihan Pharma Co, Tehran, Iran), and bupivacaine (BUP; 1 mg/kg; 5 mg/mL; AstraZeneca, Cenexi, France) was administered in epidural space, randomly. The total volume of all injections was adjusted with normal saline to 0.22 mL/kg.[2] All five animals received all the three treatments with at least one week interval.

Five minutes after epidural injection, the dogs received contrast medium via an orogastric tube. The contrast medium was a commercially available barium sulfate (Suspension, Daroupakhsh, Iran) prepared according to the manufacture`s instruction (concentration: 30% w/w) and administered at dose of 3 mL/kg.[13] Serial left lateral recumbent radiographs using Toshiba mobile x-ray unit (KCD-10M-6A1T) were taken at 0, 20, 40, and 60 minutes post administration and then every one hour till reaching the contrast medium to the colon. Thereafter, radiographs were obtained every 24 hours until the full evacuation of the contrast medium from GI tract was seen (Fig. 1). The dogs were returned to their own cage after reaching the contrast medium to the colon and accessed to food and water. In the present study all radiographs were taken without any more sedation or anesthesia except for initial administration for facilitating performing epidural anesthesia. One week after accomplishing the study, radiographs were read by an experienced radiologist who was unaware of the treatments. In the current study, onset and duration of sedation achieved by ketamine-acepromazine as well as analgesia and motor block following epidural administration were also recorded. Onset of sedation was defined as the beginning of ataxia and conscious impairment in the animals. The end of sedation was considered when the animal became alert and responsive to the circumstances. Analgesia was evaluated by applying a pinch with a haemostatic forceps (8-inch Rochester Dean Haemostatic Forceps; Martin, Tuttlingen, Germany) in the all pads of the digits of two hind legs. Motor block was also evaluated by the ability of the animals to stand on their pelvic limbs.[14] All evaluations were done with a single assessor who was blind to the treatments.

Statistical analysis was performed using SPSS software version 22 for windows (IBM SPSS statistic, IBM Corporation, NY, USA). The data are expressed as mean±SD. Time to the onset and completion of gastric emptying of the contrast medium as well as reaching the contrast medium to the colon and full evacuation of the contrast medium from GI tract was compared using the Friedman test. Onset and duration of sedation among the three groups was compared with repeated measure for ANOVA. Comparison of the onset and duration of analgesia and motor block between and within LID and BUP was performed by paired sample t-test. $P<0.05$ was considered as the significant level.

Results

Body weights were not significantly different among groups at the time of the each three treatments (20.3±2.3 kg for SAL, 20.4±4.3 kg for LID, and 19.2±3.7 kg for BUP). Mean±SD of the time to the onset and completion of gastric emptying of contrast medium as well as reaching the contrast medium to the colon and full evacuation of the contrast medium from the GI tract for each treatment were presented in Table 1. The time to the onset of gastric emptying was significantly different between treatments ($p< 0.05$). The times of the

other parameters were not significantly different among groups (p>0.05).

All the animals which received sedation and epidural anesthesia, recovered completely without any sequela. Epidural anesthesia was failed in two dogs (one in LID and one in BUP). The epidural procedure was repeated in the failed dogs one week later. The time to the onset and duration of sedation achieved by ketamine-acepromazine, analgesia, and motor block were presented in Table 2. The time to the onset and duration of sedation as well as the time to the onset of analgesia and motor block did not show any significant differences between LID and BUP (p>0.05). Duration of analgesia and motor block was significantly higher in BUP compared to LID (P<0.05). Duration of motor block was also significantly higher within LID and BUP compared to the duration of analgesia (p<0.05).

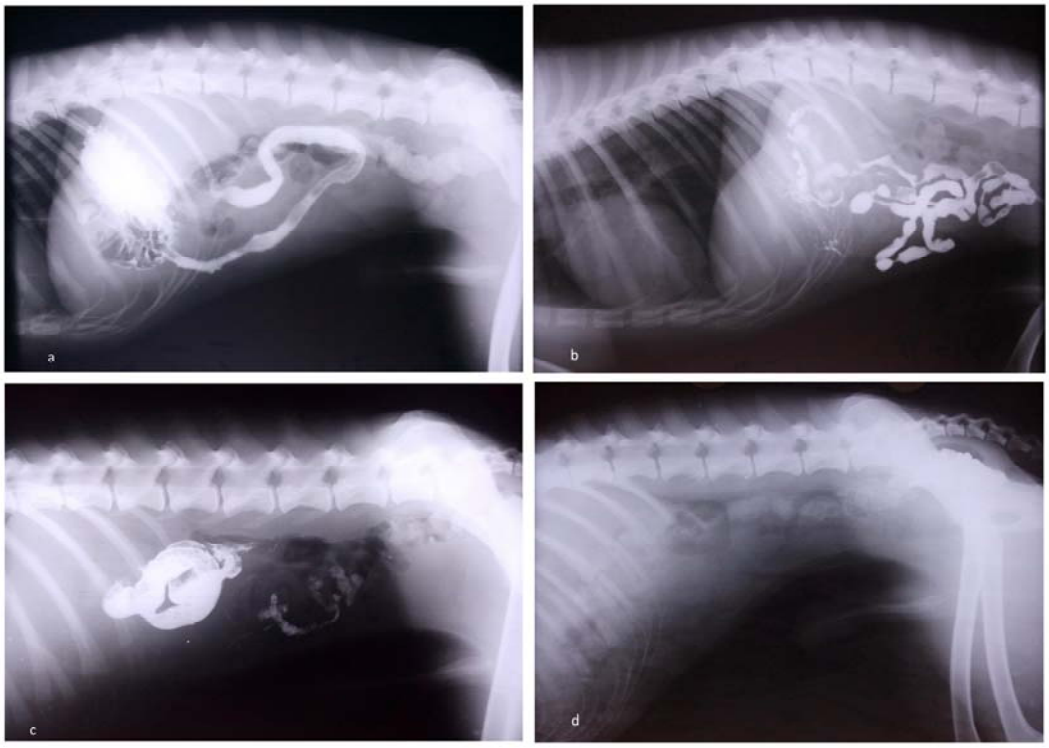

Figure 1- Serial radiographs were taken from a dog in group LID (epidural lidocaine 4 mg/kg). **a**) Onset of gastric emptying (time: 40 min). **b**) Completion of gastric emptying (time: 2 h). **c**) Reaching the contrast medium to the colon (time: 5 h). **d**) Full evacuation of the contrast medium from the GI tract (time: 48 h).

Table 1. Mean ± SD of the times to the onset and completion of gastric emptying of the contrast medium as well as reaching the contrast medium to the colon and the full evacuation of the contrast medium from the GI tract in the five dogs received epidural Saline, Lidocaine (4 mg/kg), and bupivacaine (1 mg/kg) (total volume = 0.22 mL/kg).

	Onset of gastric emptying (min)	Completion of gastric emptying (min)	Reaching to the colon (h)	Full evacuation from GI tract (h)
Saline	32.0 ± 11.0*	84.0 ± 33.0	5.4 ± 0.5	38.4 ± 13.2
Lidocaine	20.0 ± 00.0	96.0 ± 33.0	5.6 ± 0.5	33.6 ± 13.2
Bupivacaine	20.0 ± 00.0	60.0 ± 00.0	5.0 ± 00.0	38.4 ± 13.2

*Significantly different from LID and BUP (P < 0.05).

Table 2. Mean ± SD of the times to the onset and duration of sedation, analgesia, and motor block in five dogs received epidural Saline, Lidocaine (4 mg/kg), and bupivacaine (1 mg/kg) (total volume = 0.22 mL/kg).

	Sedation		Analgesia		Motor block	
	Onset (min)	Duration (min)	Onset (min)	Duration (min)	Onset (min)	Duration (min)
Saline	5.6 ± 0.9	27.2 ± 7.2	-	-	-	-
Lidocaine	7.2 ± 1.5	26.2 ± 7.1	6.4 ± 3.7	113.6 ± 7.2*	5.75 ± 0.9	133.6 ± 13.5*†
Bupivacaine	6.2 ± 1.1	27.0 ± 9.8	8.0 ± 2.1	259.6 ± 25.8	7.5 ± 1.3	305.4 ± 28.8 †

*Significantly different from Bupivacaine ($p<0.05$).
† Significantly different from duration of analgesia within each group ($p<0.05$).

Discussion

The effect of epidural anesthesia with local anesthetics on GI transit time has been evaluated in humans by several studies. Regardless to the conflicting results of these studies, all of them have been done in patients who undergone different types of abdominal surgeries.[4] Studies in veterinary medicine which evaluated with the same aim, have also been associated with abdominal surgery.[5,15] To the best of the author`s knowledge, the present study is the first experiment evaluated the effect of epidural anesthesia on GI transit time in healthy dogs. Since most studies have evaluated the effects of epidural anesthesia on perioperative period, evaluation in healthy subjects may be beneficial in the better understanding of the probable mechanisms of this method on GI function. As stated before, epidural anesthesia with local anesthetics has decreased postoperative ileus, patient morbidity, and hospital stay in human patients.[4] The results of the shortening the postoperative ileus were obtained via determination of earlier flatus and feces, bowel tone, and quicker transit of radiopaque markers.[4,5] In contrast, some studies did not show any differences in the aforementioned factors in whom received epidural local anesthetics compared to control group.[9-12] Jansen et al. (2002) showed that postoperative epidural bupivacaine could shorten the intestinal paralysis in dogs which a short segment of colon resected.[5] In the contrary to the previous study, Nakayoshi et al. (2007) did not find any differences in the first gastric interdigestive migrating complex after open abdominal surgery in dogs which received epidural ropivacaine compared to saline.[15] The variations which are seen among different studies may be related to different methods employed for epidural administration and evaluation, the time of the epidural administration, and the type as well as the concentration of the local anesthetics used by different authors.[4] According to the results of the present study epidural application of lidocaine and bupivacaine resulted in earlier onset of gastric emptying in healthy dogs. However the other factors including the completion of gastric emptying, reaching the contrast medium to the colon and full evacuation of the contrast medium from the GI tract did not show any significant differences in comparison with epidural saline.

Because of involving of various factors affect GI motility,[4,16] the exact mechanism of epidural anesthesia on GI function is not completely understood. Epidural anesthesia may increase the GI motility and inhibit development of ileus via stimulation of parasympathetic system and inhibition of sympathetic system.[4] Epidural application of bupivacaine has been suggested to have a sympatholytic effect on spinal reflex mechanisms which may play a role in shortening the postoperative paralysis.[5] In addition to direct effects of epidural anesthesia on GI motility, the nature of the drug may also be important. A number of studies in human patients have been proved the favorable effects of intravenous (IV) infusion of lidocaine on reducing the duration of postoperative ileus.[17-19] Similar results have been obtained when intra- and postoperative infusion of lidocaine administered in horses.[20] However, in the study of Milligan et al. (2007) no differences were found in jejunal motility following infusion of lidocaine in normal horses.[21]

Various methods could be employed for evaluation of transit time in the GI tract of dogs including diagnostic imaging, electrical resistance and tracer studies.[22-24] Among diagnostic imaging methods, radiography and fluoroscopy produce qualitative and quantitative data on the rate and pattern of the function of the GI tract.[16] The administration of liquid barium is the most commonly used method for assessment of GI motility and especially gastric emptying in dogs, however this method may not be useful for detection of some abnormalities of GI tract.[16,25] In the present study administration of liquid barium sulfate was employed for assessment of GI motility because of availability and relatively eases of doing the procedure in dogs.

In the present study, the time to the onset and duration of sedation following lower doses of ketamine and acepromazine did not show any significant differences among groups. Ketamine and acepromazine were used

to facilitate restraint the animal at the time of the epidural administration. Fass et al. (1995) have shown that IV ketamine resulted in no basic changes in the GI motility of dogs.[26] Continuous ketamine infusion has delayed the GI transit time in healthy horses.[27] It has been suggested, when contrast studies is required, acepromazine or ketamine may be used for sedation in cats.[28] In contrast, a study performed by Hogan and Aronson (1988) suggested that ketamine alone and in combination with acepromazine could reduce the GI transit time in cats.[29] Therefore, since no study was found that evaluated the effects of ketamine and acepromazine combination on GI motility in dogs, the possible overall effects of the aforementioned combination used in the current study should also be considered.

The onset and duration of analgesia and motor block in the current study produced by lidocaine and bupivacaine is comparable to previous studies in dogs.[2,30] The onset of analgesia and motor block was not significantly different between LID and BUP and all were seen in less than 10 min. These findings are consistent with Jones (2001) who suggested a similar onset of action of lidocaine and bupivacaine in epidural application in dogs.[30] Bupivacaine has produced more duration of analgesia and motor block compared to lidocaine which interpreted as a higher protein binding capacity of bupivacaine.[2,30] The duration of motor block in both groups was also significantly higher than analgesia as reported by previous studies.[14]

In conclusion, epidural anesthesia with lidocaine and bupivacaine could reduce the onset of gastric emptying of barium sulfate administered orally in healthy dogs. No differences were found in the completion of gastric emptying, reaching the contrast medium to the colon and full evacuation of the contrast medium from the GI tract. Further studies would be needed to determine whether this difference is clinically important.

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چکیده

تأثیر بی‌حسی اپیدورال با لیدوکائین و بوپیواکائین بر زمان عبور دستگاه گوارش سگ‌های سالم

هادی ایمانی*[۱]، عبدالواحد معربی[۱]، علی بنی‌آدم[۱]، احمد خواجه[۲]، فرشته علیپور[۳]

[۱] گروه علوم درمانگاهی، دانشکده دامپزشکی دانشگاه شهید چمران اهواز، اهواز، ایران.
[۲] دستیار تخصصی جراحی دامپزشکی، دانشکده دامپزشکی دانشگاه شهید چمران اهواز، اهواز، ایران.
[۳] دانشجوی دکتری حرفه‌ای دامپزشکی، دانشکده دامپزشکی دانشگاه شهید چمران اهواز، اهواز، ایران.

هدف- بررسی بی‌حسی اپیدورال با لیدوکائین و بوپیواکائین بر زمان عبور ماده حاجب سولفات باریم از دستگاه گوارش سگ‌های سالم.
طرح مطالعه- مطالعه تجربی آینده‌نگر
حیوانات- پنج قلاده سگ ماده نژاد مخلوط با سن ۷/۸ ± ۱۹/۲ ماه و وزن ۳/۳ ± ۱۹/۹ کیلوگرم
روش کار- حیوانات یکی از سه درمان سالین، لیدوکائین و بوپیواکائین را به صورت اپیدورال و تصادفی دریافت نمودند. حجم نهایی تمام تزریقات با استفاده از نرمال سالین به۰/۲۲ mL/kgرسانده شد. همه سگ‌ها هر سه درمان را با فاصله حداقل یک هفته دریافت نمودند. پس از تجویز دهانی سولفات باریم (۳ mL/kg)، از حیوانات در وضعیت خوابیده به پهلوی چپ رادیوگراف‌های سریالی در دقایق ۰، ۲۰، ۴۰ و ۶۰ و سپس هر یک ساعت تا زمان رسیدن ماده حاجب به کولون اخذ شد. پس از آن رادیوگرف هر ۲۴ ساعت یکبار تا تخلیه کامل ماده حاجب از دستگاه گوارش گرفته شد.
نتایج- زمان شروع تخلیه معده به صورت معنی‌داری در گروه لیدوکائین و بوپیواکائین نسبت به گروه سالین سریع‌تر بود ($p<۰/۰۵$). زمان تخلیه کامل معده، رسیدن ماده حاجب به کولون و دفع کامل ماده حاجب از دستگاه گوارش تفاوت معنی‌داری را در گروه‌های تحت مطالعه نشان نداد ($p>۰/۰۵$).
نتیجه‌گیری و کاربرد بالینی- بی‌حسی اپیدورال با لیدوکائین و بوپیواکائین می‌تواند زمان شروع تخلیه معده را در سگ‌های سالمی که ماده حاجب سولفات باریم را دریافت نموده‌اند، کاهش دهد.
کلمات کلیدی- اپیدورال، لیدوکائین، بوپیواکائین، زمان عبور، سگ.