The effect of epidural injection speed on epidural pressure and distribution of solution in anesthetized dogs

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Abstract

Objective To determine the effect of injection speed on epidural pressure (EP), injection pressure (IP), epidural distribution (ED) of solution, and extent of sensory blockade (SB) during lumbosacral epidural anesthesia in dogs.

Study design Prospective experimental trial.

Animals Ten healthy adult Beagle dogs weighing 8.7 ± 1.6 kg.

Methods General anesthesia was induced with propofol administered intravenously and maintained with isoflurane. Keeping the dogs in sternal recumbency, two spinal needles connected to electrical pressure transducers were inserted into the L6-L7 and the L7-S1 intervertebral epidural spaces for EP and IP measurements, respectively. Bupivacaine 0.5% diluted in iohexol was administered epidurally to each dog via spinal needle at L7-S1 intervertebral space, at two rates of injection (1 and 2 mL minute⁻¹ groups), with a 1-week washout period. Epidural distribution was verified with computed tomography, and SB was evaluated after arousal by pinching the skin with a mosquito hemostatic forceps over the vertebral dermatomes. The results were analyzed according to each injection speed, using paired t- and Wilcoxon signed-rank tests.

Results Mean ± SD of baseline EP and IP values were 2.1 ± 6.1 and 2.6 ± 7.1 mmHg, respectively. Significant differences were observed between 1 and 2 mL minute⁻¹ groups for peak EP (23.1 ± 8.5 and 35.0 ± 14.5 mmHg, p = 0.047) and peak IP (68.5 ± 10.7 and 144.7 ± 32.6 mmHg, p < 0.001). However, the median (range) of the ED, 11.5 (4–22) and 12 (5–21) vertebrae, and SB, 3.5 (0–20) and 1 (0–20) dermatomes, values of the two groups were not related to injection speed.

Conclusions and clinical relevance The EP profile during injection was measured by separating the injection and pressure monitoring lines. The increase in epidural injection speed increased the EP, but not the ED or the SB in dogs.

Keywords dog, epidural, injection, pressure, speed.

Introduction

Epidural anesthesia has been commonly used as a part of a balanced anesthetic protocol, for postoperative pain management in surgical cases, and to treat non-surgical pain in small animal practice (Skarda & Tranquilli 2007; Muir et al. 2013). Unfortunately, however, inadequate analgesia was sometimes experienced including insufficient range of pain relief and sensory blockade (SB) deviating from target spinal segment, and these unexpected results have motivated research to determine the influencing factors. The factors can be divided into three main groups including physical characteristics, technical factors, and epidural anatomical and physiological factors (Lee et al. 2001, 2004).
Among them, epidural pressure (EP) has been suggested as one of the epidural physiological factors since 1960s (Usubiaga et al. 1967b). In humans, several studies reported the effects of EP on epidural distribution (ED) and the extent of SB, but there have been some disagreements between authors about its significant relationship (Usubiaga et al. 1967b; Husemeyer & White 1980; Paul & Wildsmith 1989; Hirabayashi et al. 1990; Cardoso & Carvalho 1998).

The pressure in the epidural space becomes positive as fluid enters the space (Rocco et al. 1997), and increased EP is a possible cause of complications related to epidural anesthesia in human studies (Usubiaga et al. 1967a; de Jong 1981; Shah 1994). Therefore, it is necessary to determine the factors influencing EP increases in order to reduce potential complications. A human study reported that injection speed significantly correlated with peak EP (Cardoso & Carvalho 1998), but a previous study had determined no such relationship (Husemeyer & White 1980). In a recent study of dogs, Iff et al. (2007) identified that the EP increase was not related to the duration of the injection.

Consequently, additional study is needed to solve the controversy related to the change in the EP during epidural injection that involves differences in experimental conditions, individual variations in epidural anatomy, and the resistance generated by injection force in the pressure measuring system. Therefore, this study was performed to evaluate the effect of injection speed on the change in the EP in dogs, and to examine the effect of the EP on the ED and SB.

**Materials and methods**

**Animals**

All experimental procedures were approved by the Institutional Animal Care and Use Committee of Seoul National University (SNU-120222-2). The data were obtained from clinically healthy Beagles (five males and five females). Body condition score (BCS) was assessed on a 9-point scale based on previously described methods (Mawby et al. 2004). Mean ± SD body weight was 8.7 ± 1.6 kg, and the median BCS was 5, ranging from 3 to 7.

**Anesthesia and positioning**

Food was withheld for 12 hours before the experiment, but water was provided *ad libitum*. Following premedication with acepromazine (Sedajet; Samu, Median, Korea) intravenously (IV), general anesthesia was induced with propofol (4 and 2 mg kg\(^{-1}\) increments; Provive 1%; Claris, India) until endotracheal intubation was possible, and maintained with a 1.0 minimal alveolar concentration of isoflurane (Ifrane; Hana Pharm., Korea) in oxygen using a circle system. Dogs were allowed to breathe spontaneously. Hartmann’s solution (H/S; Daihan Pharmaceutical Co. Ltd., Korea) was administered at a rate of 10 mL kg\(^{-1}\) hour\(^{-1}\) IV during anesthesia.

The dorsal pedal artery was catheterized with a 22-gauge over-the-needle catheter (0.9 × 25 mm; Sewoon Medical Co. Ltd., Korea) for measurement of arterial blood pressures. The electrocardiogram, hemoglobin oxygen saturation by pulse oximetry, respiratory rate by capnometry, end-tidal carbon dioxide concentration, and arterial blood pressure were continuously monitored (Datex-Ohmeda S/5; GE Healthcare, Finland) and recorded every ten seconds throughout the procedure on a laptop computer with a S5 data recorder (Datex-Ohmeda S/5 Collet version 4.0; GE Healthcare).

Each dog was positioned in sternal recumbency, with the pelvic limbs extended cranially along the abdomen and chest to increase the interspace between the sixth and seventh lumbar vertebrae (L6-L7), and between the seventh lumbar and first sacral vertebrae (L7-S1) (Di Concetto et al. 2012). The head was placed on 5 cm thick foam padding with the neck extended in a straight line. The height of the occipital bone was parallel with that of the highest point of the vertebral column to minimize the effect of head position. The dog was maintained in this position on a sliding computed tomography (CT) table throughout the experiment.

**Epidural injection and the pressure measuring system**

Bupivacaine (Bupivacaine hydrochloride; Sigma-Aldrich, MO, USA) 0.5% solution diluted in iohexol (Omnipaque 350 I mL\(^{-1}\); GE Healthcare, Ireland) was prepared at 0.2 mL kg\(^{-1}\) dose as an epidural solution for injection into the epidural space. The lumbosacral area was aseptically prepared for epidural injection. Two spinal needles (22-gauge 38 mm; Tae-chang, Korea) were connected to an electrical pressure transducer (Auto Transducer; Acemedical, Korea) via a fluid-filled and non-distensible pressure line before epidural puncture.
The pressure profiles were displayed on the monitor screen and recorded on the laptop computer. The pressure transducer was calibrated against a mercury manometer and was placed at the level of the transverse process of the last lumbar vertebra. Epidural punctures were performed at the L6-L7 and L7-S1 intervertebral spaces by the same anesthesiologist, using each spinal needle with the needle bevel directed cranially (Fig. 1). As the needle penetrated the ligamentum flavum, a distinct 'popping' sensation was felt. After the epidural puncture, a 3-minute equilibration period was allowed before baseline pressure was measured. The spinal needle inserted at the L7-S1 intervertebral epidural space was connected via a three-way tap to a syringe pump (Pump 11 elite; Harvard Apparatus, MA, USA) that provided a constant rate injection. CE, connected to a syringe pump via a three-way tap. CE, allowed before baseline pressure was measured. The spinal needle inserted at the L7-S1 intervertebral epidural space was connected via a three-way tap to a syringe pump (Pump 11 elite; Harvard Apparatus, MA, USA) that provided a constant rate injection. The needle also measured injection pressure (IP) during injection and the remaining pressure after injection. Another spinal needle at L6-L7 was used only to measure the change in EP during the same period. The epidural solution was injected twice into each dog at rates of 1 and 2 mL minute⁻¹ under the same experimental conditions, with a 1-week washout period. The pressure profiles were continuously recorded for 5 minutes from the start of epidural injection.

**Figure 1** Diagrammatic representation of pressure measurements in the epidural space of dogs. The two spinal needles were inserted to measure the epidural pressure (a) and injection pressure (b). The needle at L7-S1 was connected to a syringe pump via a three-way tap. CE, cauda equina; CSF, cerebrospinal fluid; DM, dura mater; LF, ligamentum flavum; SC, spinal cord; L6, sixth lumbar vertebra; L7, seventh lumbar vertebra; S1, first sacral vertebra.

**Computed tomography to evaluate epidural distribution**

Dogs were scanned using a single-slice helical CT unit (GE CT/e; GE Healthcare, Japan), with a slice thickness of 7 mm and a pitch of 1.5 at 120 kVp and 60 mA. Computed tomography epidurographic images were obtained before injection and at 10 minutes after injection under the same CT conditions as the control and tested images, respectively. The longitudinal distribution along the epidural canal was determined using transsectional images, and ED was counted by the number of distributed vertebrae from the L7 vertebra: L7 = 1, L6 = 2, L5 = 3, and so forth, up to C1 = 27 (Iseri et al. 2010). The vertebra was included when the contrast medium was spread over more than a half of the vertebra. When there was unilateral distribution, each distribution of left- and right-sided around the spinal cord was counted separately, and the furthest spread was chosen as the ED value for the dog.

In addition, the point of the spinal needle at L7-S1 was scanned with a slice thickness of 1 mm to identify relationship between the lateral position of needle-tip and the unilateral distribution. A baseline for dividing the left and right side was drawn from the center of the spinous process to the center of the dorsal surface of the vertebral body on the transsectional CT image. The data were arranged as left, right, or middle position of the needle tip, to compare with left or right unilateral and/or bilateral distribution.

**Evaluation of the extent of sensory blockade**

After the CT examinations, the dogs were allowed to completely recover from anesthesia for about 20 minutes. The epidural SB was evaluated by one investigator who was blinded to the injection speed and ED. The extent of SB was assessed in three areas of the body (Lorenz et al. 2011): 1) the third bilateral pelvic toe web (L5-L7 dermatomes), 2) sacral area (L2-L5 dermatomes), and 3) the dorsal area of the ribs (thoracolumbar area; T1-L1 dermatomes). The SB at the toe web was assessed by applying hemostatic forceps, which were clamped at the first ratchet lock onto the interdigital space of the bilateral pelvic limbs. The SB on the sacral and thoracolumbar regions was tested in a caudocranial direction, using a bilateral skin pinching method (Gomez de Segura et al. 2009).
2-point rating scale was used for all areas: 1, present; 2, no response. Only complete SB was assessed, and special attention was paid to ascertain that the response of the animal to the stimulus (sudden withdrawal, head turn, or vocalization) was not due to a learned behavior, but a response to a nociceptive stimulus (interdigital or skin pinch). The SB assessment was performed when the dogs were conscious: between 30 and 40 minutes after the epidural injection. The SB dermatomes were counted using the same methods as for the ED evaluation. When there was unilateral SB, each left- and right-sided dermatome from the midline of the back was counted separately, and the furthest dermatome was chosen as the SB value for the dog.

Statistical analyses

Statistical analysis was performed using the SPSS 20 statistical program for Windows (SPSS Inc., IL, USA). Pressure data were reported as mean (± SD) values, and the ED and SB results were reported as median (range). Normality was tested by the Kolmogorov–Smirnov test. When the descriptive data were distributed normally, a paired t-test was used to compare the matched data of two groups. The Wilcoxon signed-rank test was used if the data were not distributed normally. Overall, p value of <0.05 was considered significant.

Results

Cardiopulmonary variables during anesthesia were within normal ranges, and mean arterial pressure was over 60 mmHg during epidural anesthesia in all dogs. When the spinal needle was inserted through the ligamentum flavum, the displayed pressure rapidly increased and then suddenly decreased in most dogs. Correct insertion of the needle tip into the epidural space was confirmed by CT imaging.

Mean baseline EP and IP values were 2.1 ± 6.1 and 2.6 ± 7.1 mmHg, respectively (Table 1). Mean IP profiles showed a rapid increase at the beginning of the injection and a sharp decrease after the end of the injection compared to the EP profiles in the 1 and 2 mL minute⁻¹ groups (Fig. 2). Peak IP and EP measurements in the 2 mL minute⁻¹ group were significantly higher than those in the 1 mL minute⁻¹ group (IP: p < 0.001, EP: p = 0.047, Table 1). The waves in EP and IP were synchronized with the arterial pressure wave after injection in all dogs, and no cerebrospinal fluid leakage was observed when the pressure tubing was disconnected from the spinal needle.

There was no significant difference in ED between the two groups as confirmed by CT epidurography (Table 1), but each dog had similar patterns of ED in longitudinal and transectional spread at different injection speeds. Partial unilateral distribution was observed on the cranial margin of ED in the 1 mL minute⁻¹ (right side n = 3, left side n = 6, bilateral n = 1) and 2 mL minute⁻¹ group (right side n = 6, left side n = 3, bilateral n = 1). This unilateralism was compared to the biased direction (right n = 2, left n = 17, center n = 1) of the inserted needle tip and to the peak ED, but a significant relationship was not present. Although one dog had almost unilateral distribution and SB from the injection point to the sixth cervical vertebra, cardiopulmonary abnormalities such as bradycardia, hypotension, or apnea were not recorded during and after epidural injection.

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<tr>
<th>Evaluation parameters</th>
<th>Injection speeds</th>
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<td>1 mL minute⁻¹</td>
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<td>Baseline pressure (mmHg)</td>
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<td>Maximum ED (vertebrae)</td>
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<td>Maximum SB (dermatomes)</td>
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Data are mean ± SD or median (range). *Significant difference between injection speeds (p < 0.05).
There was individual variation in SB and no significant correlation between two groups (Table 1). A significant correlation between matched ED and SB was observed ($p < 0.001$).

**Discussion**

Several studies have reported that EP measured via a needle inserted into the epidural space was changeable by posture, pregnancy and epidural injection in both humans and animals (Messih 1981; Lee et al. 2002; Iff et al. 2007). During epidural anesthesia, the epidural injection induces a substantial increase in EP, and it has been suggested as an influencing factor on ED of injected fluid (Usubiaga et al. 1967b; Hirabayashi et al. 1990). In addition, excessive increment of EP is a possible cause of complications related to epidural anesthesia in human studies (Usubiaga et al. 1967a; de Jong 1981; Shah 1994). For adequate epidural analgesia with minimal complication, it is necessary to prevent a sudden and excessive alteration of EP, and to determine the influencing factors on EP increment during injection.

Three main factors have been suggested to influence positive pressure generated by injection of a solution into the epidural space: 1) volume, 2) injection speed, and 3) epidural anatomical characteristics (Bengis & Guyton 1977; Hirabayashi et al. 1990; Cardoso & Carvalho 1998; Lee et al. 2002). In general, the injected solution increases pressure in a restricted space like the epidural space, and the severity of it necessarily depends on the volume and speed of solution injected. However, a previous study in humans reported that peak EP is not related to injection volume (Paul & Wildsmith 1989). A more recent study determined a significant relationship between volume and remaining pressure after injection in humans (Cardoso & Carvalho 1998).

Injection speed under the same volume condition has been suggested as a major factor associated with peak EP. A previous human study reported that increased EP was not related to injection time in pregnant women (Husemeyer & White 1980), but a later study indicated that peak pressures were correlated with the speed of injection of a lidocaine solution (Cardoso & Carvalho 1998). In dogs and cats, only one clinical guideline is available for injection time, stating that more than 30–60 seconds should be taken to inject epidural anesthetic agents (Jones 2001). Iff et al. (2007) reported the EP profiles generated by injection over 30 or 90 seconds with a variation in EP and no significant difference between the peak EP and injection time in dogs. In the present study, injection of 0.2 mL kg$^{-1}$ at rates of 1 and 2 mL minute$^{-1}$ resulted in 60 and 30 seconds for 1 mL per 5 kg, respectively, and the peak EP was significantly related to injection speed ($p = 0.047$). Comparing with the previous study of Iff et al. (2007), the use of constant rate injection would be necessary to control the peak EP during epidural injection. In addition, in large or obese dogs, for which the calculated volume of epidural fluid is large, maintaining the guideline of 30–60 seconds would result in a more rapid administration and a secondary EP increment. Consequently, a constant rate injection should be recommended as a standard procedure to prevent the excessive increase of EP during epidural anesthesia. Although a maximum
safe EP level has not been reported, a slower injection with constant rate would be more suitable for high risk groups of EP increase by injection, such as lumbar spinal stenosis, pregnancy, or at risk for intracranial hypertension (Messih 1981; Hilt et al. 1986; Takahashi et al. 1995).

The anatomical characteristics of the epidural canal have also been suggested as a factor influencing peak EP. The epidural canal has a compliance which depends on the composition and resistance of the tissue in the epidural space, and a leaking space at the intervertebral foramina (Rocco et al. 1997). These characteristics have been proposed as causes of wide variations observed in peak EP during injection, and as reasons for the lack of correlation between peak EP and injection speed (Husemeyer & White 1980; Iff et al. 2007). However, the significant correlation between EP and injection speed in this study minimizes the effect of epidural compliance. In fact, the experiment in the present study was duplicated in the same dog with different injection speeds in order to minimize individual variations in epidural anatomy and to identify the conditions which generated the significant relationship between EP and injection speed.

In most previous studies, epidural injection and EP measurement were performed using only one spinal needle (Husemeyer & White 1980; Paul & Wildsmith 1989; Rocco et al. 1997; Cardoso & Carvalho 1998; Iff et al. 2007). However, when EP is measured at the injection site with this method, falsely high pressure could be generated by the resistance against the injection force by the needle, the three-way tap and the needle tip in an enclosed epidural tissue. Because it was thought that this falsely high pressure may disrupt the verification of EP change according to injection speed, two spinal needles were used for separating the injection line from pressure monitoring line in this study. This was particularly important because the high viscosity of contrast medium might increase resistance during injection through the small diameter spinal needle.

The effect of peak EP on epidural analgesia was not identified in this study. When a fluid easily flows along the epidural canal, the solution may spread in association with peak EP related to its injection speed. However, the epidural space is a true potential space, which is mostly filled with connective tissue, fat, and venous plexuses (Newell 1999), and is only apparent when the dura mater is artificially separated from the overlying vertebral canal by the injection of fluid (Parkin & Harrison 1985). In addition, Hogan (2002) reported that the epidural solution spread from an area of high injected pressure to the margins of distribution where fluid pressure is low via the various passages among the epidural tissue according to the subtle forces compressing their opposing surfaces. Although elevated EP generated by the volume of injected solution plays a major role in the ED of that solution, the effect of peak EP on ED and SB would be restricted by epidural structures impeding the flow of epidural solution. In a study examining influence of volume and injection speed on epidural anesthesia in human patients, it had been reported that the injected solution might be mainly spread by remaining EP after the termination of injection more than peak EP related to its injection speed (Cardoso & Carvalho 1998).

Computed tomography provides better resolution than radiography for hydrodynamic studies of an injected epidural solution, as CT shows not only the longitudinal distribution along the epidural canal, but also the transsectional distribution around the spinal cord (Naganobu & Hagio 2007). Sternal or dorsal recumbency after epidural injection in dogs has been recommended to facilitate an even distribution and bilateral blockade (Torske & Dyson 2000; Jones 2001). Nonetheless, in almost all dogs of this study partial unilateral distribution and SB were confirmed at the most cranial dermatomes. One proposed mechanism for this abnormality in humans is unilateral distribution caused by the needle tip position (Whitlock et al. 2007). However, there was no relationship between ED and the location of the needle tip in the dogs of this study. In an epidural study using human cadavers, similar ED was reported in that the passage of ink around the dura was completely circumferential near the injection sites in most cases, but it was typical to see nonuniform spread away from injection sites (Hogan 2002). The reason for uneven distribution might be too low fluid pressure to pass between the tissues in the epidural space (Hogan 2002).

In the results of this study, although a significant relationship between ED and SB was observed, there was a substantial gap between mean ED and SB. The analgesic area is changeable according to type of nociceptive stimuli and scale of pain assessment, and evaluating the blocked area against an intense stimulus such as pinching in this study would reduce the extent of SB. In a study where bupivacaine was injected epidurally, the extent of SB was
changeable according to the passage of time, and peak ED was generated within 20 minutes from epidural injection (Freire et al. 2010). The authors tried to minimize the time gap between epidural injection and pain test for verification of the peak ED. In the present study, however, general anesthesia was essential to measure the EP during and after epidural injection, to maintain the sternal position during ED of injected solution, and to scan distribution of the injected solution with CT. Consequently, assessment of response to nociception had to be delayed until the dogs recovered from anesthesia, and the extended time gap also might have considerably influenced differences between the extent of ED and SB.

In conclusion, the EP alteration by constant rate injection was ascertained without the resistance of the pressure measuring device by separating the injection and pressure monitoring lines. The peak EP was directly correlated with the injection speed of the epidural solution in dogs, but not ED and SB.

Acknowledgements
This research was supported by the Basic Science Research Promotion program, through the National Research Foundation of Korea (NRF), as funded by the Ministry Education, Science, and Technology (2011-0007777, 2012-0002638), and the BK21 program and the Research Institute for Veterinary Science, College of Veterinary Medicine, Seoul National University.

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Received 2 July 2013; accepted 3 November 2013.