論 文 の 内 容 の 要 旨

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氏　　名　　張　迪
指導教員名　　西村　亮平

論文題目　Studies on the feasibility and safety of thoracic epidural anesthesia in dogs
（犬における胸部硬膜外麻酔の応用性および安全性に関する研究）

Epidural anesthesia and analgesia has been widely used in humans and a variety of animal species. In humans, epidural drugs are administered at various vertebral levels to provide anesthetic and analgesic effect to the target spinal segments. Thoracic epidural anesthesia is reported to provide optimal anesthetic and analgesic effect for cardiac, thoracic and upper abdominal surgery, while lumbar epidural anesthesia is more applied to surgeries involving the lower limbs, the pelvis and its organs, the groin and the pubic region. Epidural anesthesia has been also known to have the ability to improve the gastrointestinal blood flow and motility, attenuate the stress response caused by surgery or trauma, and reduces postoperative mortality and morbidity, which may improve the overall outcomes after major surgery.

In dogs, epidural anesthesia is commonly performed at caudal lumbar level or lumbosacral space in dogs, which is usually limited to surgical procedures caudal to the umbilicus, because of some anatomical concerns: unobvious landmarks and relatively narrow intervertebral spaces in thoracic vertebral region. However, it has been reported that procedures of myelography or epidurography can be performed from a thoracic vertebral tap in dogs, which suggests that epidural needle puncture and catheterization is also possible to be performed in thoracic vertebral region.

Although epidural anesthesia is known to be effective for pain relief, some technical problems and adverse effects have been reported. The incidence of serious neurological deficits was extremely low in humans, but directed needle or catheter-induced tissue trauma such as dural puncture and canalization has been reported. One of the major adverse effects of epidural anesthesia is cardiovascular depression caused by vasodilation and/or

myocardial depression mainly through sympathetic nerve blockade by a local anesthetic administered epidurally. A potential systemic accumulation of the local anesthetic resulted from the absorption from the epidural space or the leakage from the intervetebral foramina is another safety concern, because high blood concentration of local anesthetics may cause mild to severe toxicity.

Therefore, in the present study, a series of experiments were conducted to investigate the feasibility and safety of thoracic epidural anesthesia in dogs.

First, in Chapter 2, the technical safety and difficulty of thoracic epidural anesthesia (TEA) was investigated comparing with the lumbar epidural anesthesia (LEA) using healthy dogs. In group TEA, the catheter was inserted into the epidural space from cranial lumbar segments (L1-L3) with its tip placed in the thoracic vertebral region (T11-T12); in group LEA, the catheter was inserted from caudal lumbar segments (L6-S1) with its tip placed at mid lumbar vertebral segments (L3-L5). Epidural catheter was placed into the target epidural space successfully in all dogs. No statistical difference was observed in the time consumed for the whole process of epidural catheterization (needle puncture, catheter placement and advancement, and saline injection) between two groups. Subcutaneous blood was detected in 3 dogs of group TEA, but in no dog of group LEA. Neither macroscopic injuries such as tissue bleeding, dural puncture and canalization, nor histopathological changes were observed in any dogs. Subjective evaluation score of the overall technical difficulty was significantly higher in group TEA, however the difference was slight and the technique of epidural catheterization in thoracolumbar vertebral region could be improved after being well practiced. The findings obtained in this study supposed that the thoracic epidural anesthesia is feasible to be performed in medium or large-sized dogs in clinical settings.

In chapter 3, the spreading pattern of contrast medium epidurally administered via a catheter was studied. It has been reported that epidurography using contrast medium can be used to evaluate the distribution of local anesthetic in the epidural space, moreover computed tomograohic (CT) epidurography allows for tomographical imagine of the spinal cord. Therefore, in the first part of this chapter, by means of CT epidurography, the distribution of contrast medium epidurally injected at thoracic (group TEA) or lumbar (group LEA) vertebral level was compared. After injecting a single dose of 0.2 ml/kg contrast medium, no difference in the cranial number of vertebral segments reached by contrast medium was observed between two groups. Three possible causes may contribute to this result. First, there was less caudal space for contrast medium spreading in group LEA because of its caudal epidural injection site. Second, potential different pressure gradients between thoracic and lumbar vertebral segments, which was presumably lower in thoracic vertebral, may also facilitate the cranial spreading in group LEA. Third, contrast medium was more likely to leak out of the epidural space through the enlarged intervertebral foramina in cervicothoracic region, consequently resulting in the cranial epidurographic distribution generally limited to 5th and 6th cervical vertebral level in both groups. In other aspect, changes in the maximal CT value of the epidural space indicated that contrast medium mainly distributed at thoracic vertebral segments in group TEA, while distributed at lumbar vertebral segments in group LEA. It was implied that epidural anesthesia performed at low thoracic level may be effective for surgeries involving thoracic and upper abdominal regions. It has also proved that lumbosacral epidural anesthesia is suitable for surgeries caudal to the umbilicus.

In the second part of this chapter, a comparison of the epidural distribution of contrast medium administered at thoracic vertebral level between a single dose (group Bolus) and a continuous infusion (group CRI) was conducted. There was no difference in the number of vertebral segments reached by contrast medium between two groups. However, the contrast medium was more likely to leak out of the epidural space when drug was continuously infused. The maximal CT value decreased generally in a time-related manner in group Bolus, whereas, it kept almost stable in group CRI. This finding indicates that epidural continuous infusion is superior to a single dose injection in keeping a stable concentration of drugs distributed to the target spinal cord segments for long time surgery and postoperative analgesia. However care should be taken for systemic absorption of a drug when it is administered continuously at higher dose rate, which may contribute to the systemic toxicity.

As epidural anesthesia is usually used combined with general anesthesia in dogs especially during surgery, the evaluation of cardiovascular changes under general anesthesia is clinically important. Therefore, in chapters 4 and 5, cardiovascular effect of thoracic epidural anesthesia was studied in dogs anesthetized with inhalation anesthesia (isoflurane) or intravenous anesthesia (propofol).

In chapter 4, cardiovascular effects of two epidural techniques: thoracic epidural anesthesia (group TEA) and lumbar epidural anesthesia (group LEA) was compared after epidurally injecting a single dose of lidocaine (4 mg/kg). Under isoflurane anesthesia, arterial blood pressure mildly decreased in group TEA, with less decreasing degree than that in group LEA. Since the result showed a comparable systemic vascular resistance between two groups, changes in the stroke volume was supposed to be the major determined factor in the changes of arterial blood pressure. Overall, under isoflurane anesthesia, the myocardial function was less depressed by thoracic epidural anesthesia compared with lumbar epidural anesthesia. Under propofol anesthesia, the changes in arterial blood pressure showed a similar trend but with significantly high levels in both groups compared with those under isoflurane anesthesia, which might be related to the different cardiovascular effects of these two general anesthetics. Regardless of general anesthetics, arterial blood pressure was only mildly depressed after a single dose of lidocaine injected epidurally in thoracic vertebral region compared with lumbar vertebral region. Hence, in terms of cardiovascular effect, thoracic epidural anesthesia epidural is safe to be used in clinical settings. Under propofol anesthesia, although the arterial blood pressure was well maintained, moderate, or occasionally severe muscle tremors were observed in some dogs in both TEA and LEA groups. Therefore, propofol infusion combined with epidural anesthesia seems hardly to provide a stable condition for surgical manipulations. Some adjuvant such as systemic opioids which is commonly used for the “balanced anesthesia” may be necessary. While isoflurane inhalation combined with epidural anesthesia, under which arterial blood pressure was lower but within a clinically acceptable range, could provide a stable condition for surgical manipulations.

Finally, in chapter 5, the cardiovascular effect of continuous epidural infusion of 2% lidocaine in thoracic vertebral region was compared at three infusion rates: 0.1, 0.2 and 0.4 ml/kg/h (group 0.1, 0.2 and 0.4), respectively. Under isoflurane anesthesia, differences were not significant, but there was a dose-dependent decreasing trend in heart rate, arterial blood pressure, cardiac output and stroke volume during continuous epidural infusion, while, it was not found in systemic vascular resistance. Compared with other two infusion rates, cardiovascular variables were more depressed when a high infusion rate (0.4 ml/kg/h) was used. Similar

cardiovascular changes were also obtained in three infusion groups under propofol anesthesia. However, arterial blood pressure was significantly higher under propofol anesthesia in each group, which was thought to be attributed to the high systemic vascular resistance under propofol anesthesia. In the present study, changes in serum lidocaine concentration were similar between isoflurane and propofol anesthesia. It reached a steady state approximately at 15 min after the start of continuous infusion, and was maintained in group 0.4. In this study, the highest value was 3.3 μg/ml in group 0.4, which probably induces a mild myocardial toxicity in conscious humans. Considering cardiovascular effect, epidural continuous administration of 2% lidocaine should be infused at a rate less than 0.4 ml/kg/h in dogs.

In conclusion, comparing with the lumbar epidural anesthesia, thoracic epidural anesthesia was not technically difficult, and was feasible to be performed in medium or large-sized dogs. After epidurally injecting a single dose of lidocaine, thoracic epidural anesthesia only mildly depressed cardiovascular variables. During continuous epidural anesthesia, there was a mild to moderate dose-dependent cardiovascular depressant effects. A potential systemic lidocaine absorbed from or leak out of the epidural space may also contribute to cardiovascular changes when infused with a high rate. Results of the present results implied that, in view of clinical application, combined with isoflurane general anesthesia, epidural continuous infusion using 2% lidocaine at a rate of 0.2 ml/kg may be optimal.