A new model for the pharmacokinetic and pharmacodynamic analysis of epidural administered drugs in sedated dogs

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Introduction

-Many studies have evaluated the epidural pharmacokinetic and pharmacodynamic profiles in animal studies.

-Yaksh developed a study model in dogs [1]. He threaded two catheters, one caudally around the cisterna magna into the intrathecal space and the other at the lumbosacral area upward into the epidural space to meet the two catheters at the same spinal level.

-However, in this method, some problems can occur such as bleeding and spinal cord damage due to the long trajectory of epidural catheter for adequate placement of epidural level.

-Here we present a novel model, non-surgical and less invasive for the pharmacokinetic and pharmacodynamic analysis of epidural administered drugs.

Materials and Methods

The study was conducted after institutional approval for animal experiment by the Korea University Institutional Animal Care and Use Committee. Twelve dogs weighing 21 kg (21 ± 2.77 kg; mean $\pm$ SD) were used.

Epidural catheterization

The 17G Tuohy needle was inserted into the T1-2 intervertebral space. The Tuohy needle was inserted targeting the T1-T2 intervertebral space. The “loss of resistance to air (LOR)” technique was used to confirm the epidural space (Fig 1A). As the needle placed into the epidural space confirmed by the loss of resistance technique, a catheter was advanced cephalad through the needle to the C2-C3 level (Fig 1B). After confirming correct placement at the epidural space using fluoroscopic images, the needle was removed and the indwelling catheter was placed (Fig 1C).

Fig. 1. Thoracic Epidural catheterization in dog.

Intrathecal catheterization

In the lateral position, the external occipital protuberance, as well as both tips of the transverse processes of C1, was located using palpation; these three points formed the vertices of a triangle and the center of a triangle was a target point (Fig. 2). Under local anesthesia, a 17G Tuohy needle was inserted into the cisterna magna region, checking the midline. A flexible catheter was then inserted caudated through the needle to the C2-C3 level; that is, to the same level as the epidural catheter.

Fig. 2. Intrathecal catheterization in dog.

Result

The Tuohy needle was inserted in epidural space at the T1-T2 intervertebral level using the LOR technique and the needle position was confirmed by fluoroscopic images. It is necessary that the Tuohy needle was inserted at the midline because the internal vertebral venous plexus could be damaged during the procedure, if the needle was not inserted at the midline (Fig.3A). We confirmed the tip of the epidural catheter and intrathecal catheter were located at the same spinal level C2-C3 in the lateral fluoroscopic images after injection of contrast dye (Fig. 3B).

Fig. 3. Serial fluoroscopic images of anteroposterior (A) and lateral images (B).

Discussion

CSF drains into the cisterna magna, so cisterna magna contains sufficient CSF collection and has been used to sample of CSF. Yaksh et al. [1] exposed the dura between the foramen magnum and the first cervical vertebra. However, in this method, it needed to surgical opening to expose the dura and general anesthesia with intubation in dogs.

We inserted intrathecal catheter into the cisterna magna by LOR technique without surgical procedure. In our study, after palpating external occipital protuberance and both transverse processes of C1, authors draw a hypothetical triangle that meets three vertices and inserted intrathecal catheter in the center of a triangle by LOR technique using 18G Tuohy needle. It is absolutely convenient for both the researcher and the animals because it is not needed surgical procedure and general anesthesia with intubation during procedure.

This model was useful for studying to compare effect of drug epidural and other administration routes and evaluating the pharmacokinetic profiles about drugs administered epidurally.

Reference

1. Durant PA, Yaksh TL. Distribution in cerebrospinal fluid, blood, and lymph of epidurally injected morphine and inulin in dogs. *Anesth Analg* 1986;65: 583-592.