Appendectomy in Rabbits with Extended Unilateral Anesthesia

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Abstract: Thoracic paravertebral anesthesia was not believed to accompany numbness in the lumbar nerve region. However, we recently discovered that thoracic paravertebral anesthesia could produce analgesia in the lumbar region. We called this block extended unilateral anesthesia. In this study, appendectomy was attempted in rabbits with extended unilateral anesthesia. After a catheter was inserted into the endo- thoracic fascia in the paravertebral region on the right side at the level of the 11th thoracic vertebra, a 3-ml dose of 2% mepivacaine was injected repeatedly through the catheter. After an injection of the local anesthetic we could observe motor and sensory paralysis unilaterally from the chest down to the lower limb in all the rabbits, the extended unilateral anesthesia. With this anesthesia, we could accomplish appendectomy. This is the initial report of extended unilateral anesthesia applied to appendectomy in rabbits. We think that this anesthesia could be beneficial in future medical and veterinary use.

Key words: anesthesia; local, endo- thoracic fascia, extended unilateral anesthesia, unilateral anesthesia

Introduction

We have previously reported a case in which the injection of local anesthetic in the paravertebral region at the T11 vertebral level gave rise to extended unilateral analgesia in thoracic and lumbar dermatomes [9]. After this clinical experience, we conducted anatomical studies to clarify the mechanisms behind our observation [10, 11]. We found that dye, a substitute for the anesthetic agent, injected at the same sites in cadavers as that in the clinical case not only spread on the same side of the paravertebral region in the thorax but also reached the transversalis fascia in the abdominal cavity through medial and lateral arcuate ligaments. A large number of nerve roots were directly affected by the dye injection.

Our next step was to repeat animal studies with this type of anesthesia. We injected local anesthetic into the same site in rabbits. We observed the same extended unilateral block, with which we successfully performed colostomy surgery [12]. To examine this anesthesia in humans, we applied this technique in patients presenting for henniorrhaphy. This sole anesthesia was adequate in nine of 15 patients for henniorrhaphy.

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In one of the six patients for whom this anesthesia was inadequate the anesthetic had obviously been wrongly deposited. We postulated that the anesthetics were injected in the wrong place because we had only little kinesthetic experience of needle insertion. We did not know the precise anatomic structure for the proper deposition at that time and yet. We agreed that kinesthetic experience was very important, and concluded that it was necessary to return to an animal study to achieve an understanding of kinesthetics before further human study.

We also had another interest in this study. In previous studies we examined the extended unilateral anesthesia on the left side. Although it is mandatory to perform anesthesia on the right side for the maintenance of anesthesia in appendectomy, the paravertebral regions on the right and left sides are different because the aorta passes down the left side. In this study we examined the characteristics responses of both sides of the paravertebral region to anesthesia, and report how this type of anesthesia was successfully used for appendectomy on rabbits.

**Methods**

The study was approved by the Ethical Committee in Research Methods of the Nippon Medical School (Approval No. 11–55). Eight female rabbits (body weight 3 kg) were subjected to the study. The rabbits were evaluated for normal gait and sensory responses as described below prior to any surgical procedures.

**Experimental Procedure**

Before anesthetic manipulation, animals were fasted over night but had free access to water. Induction of anesthesia was done with inhalation of sevoflurane. When animals lost righting reflexes, they received an i.m. injection of medetomidine hydrochloride (50 mg/kg) and sevoflurane was stopped. Thereafter anesthesia was maintained with medetomidine injection. All animals were monitored for ECG and heart rate. After an intravenous line was placed, they received intravenous fluid at a rate of 10 ml/hr.

Each animal was placed in the left lateral position, and their back was shaved and soaked in a povidone-iodine antiseptic solution. A 17-gauge Tuohy needle was inserted at the T11 level. The skin puncture was 1 cm lateral to the midline. The direction of the needle was similar to that described by Bonica for paravertebral block [2, 13]. The needle was perpendicular to the skin in the longitudinal axis and directed 105 degrees to the sagittal plane (Fig. 1). The needle had a syringe connected to it, and loss of resistance technique was used to find a site into which we could inject local anesthetic and place an epidural catheter. When the needle tip reached the space just behind the endothoracic fascia, an obvious loss of resistance was felt. A 20-gauge open-tip catheter (Hakko, Tokyo, Japan) was threaded through the needle. The catheter tip was inserted to a depth of 2.5 cm. The tip of the catheter was advanced cranially. Because rabbits are small and their tissue is soft, inserting the catheter too deep causes a higher segmental block and a higher risk of puncture of the pleura. The needle was then removed, with the catheter left in place.

Three milliliters of 2% mepivacaine was injected through the catheter. After the injection of mepivacaine, 600 µg of atipamezole hydrochloride (200 µg/kg) were administered intravenously to antagonize the effect of medetomidine hydrochloride.

At 15 and 30 min after the injection of atipamezole, the extent of the motor and sensory block was examined. Motor block was defined as the inability of the animal to support its own weight on its hind limbs. Sensory block evaluation was employed using the pan-
niculus reflex overlying each vertebral segment on both the right and left sides of the midline with Allis forceps and observing for the “fly flicker” skin twitch [3].

Using the panniculus reflex, when the upper border of the block was higher than T6 and the lower border lower than L3 in the right side, an appendectomy was attempted. Because the anesthetic was thought to spread in the unilateral paravertebral space, we did not expect any analgesia on the left side. The appendectomy was that of the standard surgical procedure except for the skin incision and the rabbit’s large cecum. A long para-rectal incision was made to create an adequate operative field. The meso-appendix was ligated and divided and the appendix was divided, close to its origin. Simple ligation of the stump and a purse-string suture were carried out. Rabbits were observed continuously during the surgery. Rabbits’ responsive movements were evaluated frequently. Two milliliters of 2% mepivacaine were injected through the inserted catheter if the rabbit showed painful behavior during the surgery. The appendectomy recommenced when we identified the resumption of the unilateral block.

After the appendectomy was accomplished, we injected 4 ml of a latex blue dye through the catheter to examine the spread of the mepivacaine. Rabbits were sacrificed by an intravenous injection of a lethal dose of pentobarbital sodium. Postmortem examinations were done, and consisted of careful dissection of the lower thoracic and lumbar paravertebral space. Spreading of the dye, and the position of the catheter as well as any visible lesions were noted.

Statistical analysis of the data consisted of analysis of variance and the Tukey HSD test. Statistical significance was recognized at the p<.05 level. Data are expressed as mean ± SD throughout the text; sample size is 7 unless otherwise noted.

### Results

Although eight female rabbits were subjected to this study, one rabbit was excluded from the data evaluation (rabbit No. 2 in Table 1). This rabbit was prepared for the study and was injected with the anesthetic, but in the autopsy process, the catheter tip was found in the chest cavity instead of the paravertebral region. The catheter had speared the parietal pleura. The rabbit’s pleura had been torn by the for-human-use-only epidural catheter.

In the remaining seven rabbits 3 ml of 2% mepivacaine caused unilateral analgesia. The extent of the nerve block examined with Allis forceps is shown in Table 1. After fifteen minutes the depth of motor block was still faint in all rabbits. When the rabbits tried to run away, their legs were still able to assist the body, but their coordination was affected. Four of the seven rabbits showed block in the panniculus reflex. After 30 min the analgesic area became obvious, and we could determine that the analgesia had extended unilaterally. Its average upper border was T3 and the lower border was L5. We did not observe any analgesic region on the left side in any of the rabbits. By this time, none of the rabbits could stand on their own rear

### Table 1. Extent of Sensory and Motor Neuron Block

<table>
<thead>
<tr>
<th>Rabbit No.</th>
<th>Extent of Motor Block</th>
<th>Extent of Sensory</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before</td>
<td>15</td>
</tr>
<tr>
<td>1</td>
<td>None</td>
<td>S</td>
</tr>
<tr>
<td>2</td>
<td>Ommitted</td>
<td>S</td>
</tr>
<tr>
<td>3</td>
<td>None</td>
<td>S</td>
</tr>
<tr>
<td>4</td>
<td>None</td>
<td>S</td>
</tr>
<tr>
<td>5</td>
<td>None</td>
<td>S</td>
</tr>
<tr>
<td>6</td>
<td>None</td>
<td>S</td>
</tr>
<tr>
<td>7</td>
<td>None</td>
<td>S</td>
</tr>
</tbody>
</table>

*S:* Rabbit could stand on her rear legs. *N:* Rabbit couldn’t stand. ( ) : extent of analgesia was not obvious. We did not observe any analgesia on the left side.
legs. Five of the seven rabbits could not move their right legs after 30 min (Fig. 2). Clipping with the Allis forceps did not cause any movement or change of respiration.

All seven rabbits were subjected to appendectomy. There were no remarkable events in the appendectomy except for the larger size of the rabbit cecum compared to that of humans. The surgical manipulation started 30 min after the injection of the anesthetic in all rabbits, and continued for 40 to 90 min (rabbit No. 6). At the 80 min-period after the injection one rabbit moved its front leg as an agonal response to a surgical stimulus. We judged the sign as a termination of the anesthesia. We injected an additional dose of mepivacaine, 3 ml, through the catheter. It required twenty min to confirm the resumption of analgesia. We then started the maneuver again and we checked the analgesic extent at 5 min intervals. We successfully finished the appendectomy without any further event with this unilateral anesthesia. The ECG and heart rate showed no remarkable change before or during the surgical manipulation.

In the postmortem examination we observed the spreading of the blue dye injected through the catheter under the parietal pleura in the chest cavity and the retroperitoneum in the abdominal cavity (Fig. 3). The spreading of the dye in the extended unilateral anesthesia on the right side was symmetrically the same as that of the left side in our previous report, although the

Fig. 2. Picture showing that the rabbit’s right rear leg was flaccid. She could not stand on the right leg after 30 min.

Fig. 3. (a) Dye spreading in the rabbit in the postmortem examination. (b) Illustration of the dye spread. The dye was found to spread in the paravertebral region unilaterally, and reached the abdominal cavity through the medial and lateral arcuate ligament at the diaphragm.
diffusion around the aorta may be a little different if examined in more detail. The tip of the catheter was found behind the parietal pleura in the chest cavity in all rabbits except the one already mentioned above.

**Discussion**

**Success rate**

In the previous study of herniorrhaphy in humans, the absolute success rate was 60% in that the anesthesia required neither additional analgesia nor sedation [13]. Twenty percent of the patients required sedatives although 80% of them finished the surgical procedure mainly with this extended unilateral analgesia. In the current study all the rabbits showed extended unilateral palsy. The high success rate in the study implies possible future clinical applications.

**Laterality**

An anatomical view showing the paravertebral space at T11 level is shown in Fig. 1. The paravertebral space is not the same on both sides. The paravertebral space has the aorta running down through it on the right side. Because of this the left paravertebral space is wider. The former accomplishment of an artificial anus formation in the animal study with extended unilateral anesthesia on the left side did not necessarily assure the usefulness of right side unilateral anesthesia [12]. It was speculated that the catheter insertion would maybe be more difficult in the right side paravertebral space. In actuality the catheter spared the parietal pleura in one rabbit and the rabbit was omitted from the evaluation. The catheter used was "only-for-human-use" for the epidural space, and its size and consistency are obviously not suitable for soft and small rabbit tissue.

**Spreading in the Paravertebral Region**

Drug diffusion in the paravertebral region has not been well studied. MacIntosh and Mushin [7] described reports in cadavers, in which there was no continuity of the paravertebral space between vertebral segments. This was confirmed by other investigators [1, 4]. Conversely, Eason and Wyatt [5] demonstrated that thoracic paravertebral block could be achieved over three to four dermatomes. Bonica [2] also found that a large volume of anesthetic solution could cause extended thoracic paravertebral block. This was also confirmed by Tenicela, and Pollans [14]. Lönqvist and Hildingsson [6] reported that the thoracic paravertebral space was separated from the lumbar paravertebral space by the psoas muscle.

Contrary to the observation by Lönqvist et al., the sequence of our studies has shown that local anesthetic and alternative dye injected at the T11 level in the paravertebral region were distributed both within the thoracic cavity and the abdominal cavity [9–13].

**In which layer in the paravertebral region did the drug diffuse?**

We are not aware in which layer in the paravertebral region the drug diffuses. In an anatomical explanation we have insisted that the drug diffused in the endo- thoracic fascia. Basically the region behind the peritreal pleura in the paravertebral region is called the endo- thoracic fascia (Fig. 4-a). In this sense the drug diffused in the endo- thoracic fascia. However, there are two layers in the parietal pleura, the parietal serous membrane and the parietal visceral fascia and one layer between the parietal pleura and the endo- thoracic fascia, the inner-most investing layer of deep fascia (I.I.L.O.D.F) (Fig. 4-b). The fact that we could observe the blue dye diffusing through the parietal pleura means that the anesthetic might have diffused within the IILODF. This layer is possibly different from that described by previous researchers.

This block is very possibly different from previously described paravertebral blocks.

**Sedation**

In this study we used medetomidine and atipamezole to wake the rabbits so that we could examine the analgesic extent produced by mepivacaine. Although it is known that atipamezole does not reverse the anesthetic effect produced by medetomidine and that mepivacaine causes a sedative effect when it is diluted in the blood circulation, we were not aware whether the rabbits were adequately sedated, although ECG and HR did not show any remarkable change reflecting a sympathetic condition. Adequacy of the sedation level for the experiment of local anesthesia should be investigated in the future.
Fig. 4. (a) Diagram of the paravertebral region. The endothoraic fascia lies between the parietal pleura and rib or respiratory muscle. (b) Closer view of the attachment of parietal pleura to endothoraic fascia. There are two layers in the parietal pleura and one layer between the parietal pleura and endothoraic fascia.

Conclusion

All rabbits injected with local anesthetic in the right paravertebral region showed unilateral anesthetia of the same side. This anesthetia was adequate for appendectomiy. We suspect that this anesthetia would be beneficial for some surgery or pain control in the abdominal region. Further investigations are required.

References