J Anesth (2004) 18:250–256
DOI 10.1007/s00540-004-0262-4

Journal of
Anesthesia



# Ropivacaine produces sensory blockade in the lumbar sacral region more frequently than mepivacaine in lower thoracic epidural anesthesia

Manzo Suzuki, Kikuzo Sugimoto, and Yoichi Shimada

Department of Anesthesiology, Second Hospital Nippon Medical School, 1-396 Kosugi-cho, Nakahara-ku, Kawasaki 211-8533, Japan

**Abstract**
*Purpose.* The first sacral nerve has the largest diameter among the spinal nerves and is resistant to local anesthetics. Ropivacaine is a newly developed local anesthetic. There is a possibility that a difference in chemical properties between ropivacaine and other local anesthetics produces a difference in the blockade of the S1 dermatome by lower thoracic epidural anesthesia. Mepivacaine, 2%, is frequently used for epidural anesthesia and produces a level of blockade similar to that of bupivacaine, 0.5%. The purpose of this study was to examine the sensory blockade in the sacral region induced by ropivacaine with that induced by mepivacaine administered in the lower thoracic epidural space.
*Methods.* Eighteen adults undergoing lower thoracic epidural anesthesia (thoracic 11/12 interspace) were studied in a double-blind fashion. Patients were assigned to one of two groups: those who received 2% mepivacaine, 18 ml (group M; $n = 9$), and those who received 1% ropivacaine, 12 ml (group R; $n = 9$). The cephalad levels of sensory blockade to cold, pinprick, and touch in the L2, S1, and S3 dermatomes were assessed at 10, 20, and 35 min after injection.
*Results.* There were no differences in the cephalad levels of sensory block to cold (T4 [range, T4–T2] and T4 [range, T6–T2]), pinprick (T4 [range, T6–T4] and T4 [range, T6–T4]), or touch (T6 [range, T6–T4] and T6 [range, T6–T4]) between group M and group R respectively, at 35 min ($P > 0.05$). In the L2 and S3 dermatomes, there were no significant differences in the numbers of patients who obtained sensory block to cold or pinprick at 20 and 35 min after study drug administration. However, in the S1 dermatome, significantly higher numbers of patients in group R obtained sensory block to cold at 20 and 35 min after study drug administration than in group M (8 and 0; 9 and 0; $P = 0.001$ and $P < 0.001$; 20 min and 35 min after administration, respectively). Also in the S1 dermatome, significantly higher numbers of patients in group R obtained sensory block to pinprick at 20 and 35 min after study drug administration than in group M (6 and 0; 9 and 0; $P = 0.027$ and $P < 0.001$; 20 min and 35 min after administration, respectively). A significantly higher number of patients in group R had sensory block to touch in the S3 dermatome at 35 min (7 and 2; group R and group M, respectively; $P = 0.01$).
*Conclusion.* Ropivacaine, 1%, administered in the lower thoracic epidural space, induces sensory blockade to cold and pinprick in the S1 dermatome more frequently than 2% mepivacaine.

**Key words** Epidural anesthesia · Sacral spread · Local anesthetics

## Introduction

The onset of blockade of impulses by a local anesthetic is affected by both the diameter of the nerve fiber and whether it is myelinated [1]. The first sacral nerve possesses the largest diameter among the spinal nerves and is relatively resistant to local anesthetics [2]. Upon epidural administration of a local anesthetic in either the lumbar or thoracic epidural space, there is a time lag in achieving sensory analgesia in the sacral nerves [3]. The sacral nerves innervate visceral organs such as the upper vagina, parametrium, and visceral peritoneum, and nociceptive input travels through intact sacral nerves during or after surgery [4]. Although lower thoracic epidural anesthesia is frequently used for perioperative pain management in lower abdominal surgery, the onset and spread of analgesia in the sacral region have not been studied.

Ropivacaine is a newly developed, long-acting amide local anesthetic that differs structurally from bupivacaine, in that the butyl group in bupivacaine is substituted by a propyl group, and ropivacaine is prepared as an S isomer rather than as a racemic mixture [5]. These differences result in an anesthetic that is less lipid-soluble and less potent than bupivacaine and of low cardiotoxicity in both animals and humans. Because of these advantages, ropivacaine can be administered in large doses with fewer cardiovascular or central nervous

*Address correspondence to*: M. Suzuki
Received: January 9, 2004 / Accepted: June 30, 2004

side effects. Because local anesthetics that are administered in the epidural space penetrate intrathecally and exert anesthetic action, the characteristics of a local anesthetic (i.e., its dissociation constant, molecular weight, and hydrophilicity) may influence the onset of its action. At our institute, 2% mepivacaine has been frequently used for epidural anesthesia. A clinical report suggested that 2% mepivacaine produces a level of blockade similar to that of 0.5% bupivacaine [6]. However, no study has compared the extent of sensory blockade in the sacral region upon lower thoracic epidural anesthesia induced by 2% mepivacaine and that induced by 1% ropivacaine. We hypothesized that the onset and spread of sensory analgesia to the sacral nerves upon lower thoracic epidural anesthesia using ropivacaine may differ from these features using mepivacaine. The purpose of this study was to examine the sensory blockade in the sacral region induced by ropivacaine administered in the lower thoracic epidural space.

## Methods

Eighteen adults receiving epidural anesthesia for lower abdominal surgery were recruited for this double-blind, randomized, mepivacaine-controlled, two-group parallel study. This study was approved by the Institutional Review Board of Second Hospital Nippon Medical School. Written informed consent was obtained from each patient. Exclusion criteria were: known allergy to local anesthetics, refusal to participate, morbid obesity, patients who were taking drugs affecting the central nervous system, diabetes, and patients with malposition of the epidural catheter during evaluation of analgesia. Patients were randomly assigned to one of two groups: group M received 2% mepivacaine; and group R received 1% ropivacaine. The drug was injected into the epidural space. An envelope that contained the group assignment, done by computer-generated randomization, was given to a nurse who did not participate in the evaluation of analgesia, and the nurse prepared the local anesthetic for the study in unlabeled vials according to assignment. The anesthesiologists who performed the epidural anesthesia and assessed the development of analgesia were unaware of the assignment. Premedication consisted of intramuscular administration of 25 mg hydroxyzine and 0.5 mg atropine sulfate, 30 min before the induction of anesthesia. In the operating room, the right anterior cubital vein was secured for intraoperative administration of acetate Ringer solution, at 7–10 $ml \cdot kg^{-1} \cdot h^{-1}$. A routine monitoring device, including ECG monitoring, noninvasive monitoring of blood pressure, and a pulse oximeter was attached. With the patient in the right lateral decubitus position, an epidural catheter (Hakko catheter for epidural anesthesia; Hakko Shoji, Tokyo, Japan) was placed via the paramedian approach by the loss-of-resistance technique to saline at the thoracic 11/12 interspace. The volume of study drug was determined by the formula: $y = 3.021\ x - 0.274\ x2 + 0.009673\ x3$, where $y$ is the number of anesthetized dermatomes and $x$ is the injected volume [7]. The volume of study drug to be administered to obtain 14 anesthetized dermatomes was calculated to be 12 ml. We decided to inject 1% ropivacaine at a volume of 12 ml. The extent of blockade by an epidural local anesthetic depends on the dose of the drug. To optimize the difference in potency between the two drugs, we injected 2% mepivacaine at a volume of 18 ml.

### *Clinical procedure*

After the baseline values of vital signs were recorded, another investigator, who was not involved in the anesthesia procedure or in the evaluation of sensory blockade, entered the operating room to inject the study drug, which was contained in a 20-ml syringe. The anesthesiologist who performed epidural anesthesia and evaluation of sensory block could not assess the identity of the study drug. After negative aspiration of cerebrospinal fluid (CSF), 3 ml of the study solution was administered over 5 s through the catheter. After 5 min, in the absence of any signs of subarachnoidal or intravenous injection, such as hypotension or arrhythmia, the remaining bolus of the study drug was administered over 3 min. The end of the injection of the remaining dose of study solution was set as time 0. During the study, a patient who developed bradycardia or hypotension with a heart rate or blood pressure below 80% of the respective baseline value was treated with intravenous bolus administration of 0.5 mg atropine or 6 mg ephedrine, respectively

### *Assessment of sensory block*

Sensory block to cold (alcohol swab) was assessed at the levels of the T2, T4, T6, T8, T10, T12, L2, S1, and S3 dermatomes at 10, 20, and 35 min after administration of the study drug. Sensory block to pinprick (18-gauge needle) and touch (dry swab) were assessed at the same levels as cold sensation at 20 and 35 min after administration of the study drug. Patients were given a reference sensation of pinprick and cold at the C5–C6 dermatome before each measurement. In the assessment of sensory block to touch, detection of the dry swab in the C5–C6 dermatome was confirmed. A dermatome was considered to be free of sensory block to pinprick or cold if that sensation was reported to be the same as the reference sensation. A dermatome was

considered to be free of sensory block to touch if the dry swab could be detected. After giving the reference sensation, the dermatomes were assessed bilaterally for sensory block, moving from a blocked to an unblocked area in the order of cold, pinprick, and then touch. To exclude conflicting results due to catheter malpositioning, patients who could not obtain sensory analgesia to either pinprick or cold at the T8 dermatome 20 min after injection were excluded from the study; it was considered either that the epidural catheter was malpositioned or that it had migrated. Sensory block to pinprick, cold, or touch was recorded as the number of dermatomes cephalad to the T11 dermatome with blocked sensation. Sacral spread was assessed as the block of sensation to pinprick, cold, or touch at the levels of the L2, S1, and S3 dermatomes. The parameters analyzed in this study were the numbers of patients who obtained sensory block in the sacral region at 10, 20, and 35 min after injection. At 40 min after administration of the study drug, and after all measurements had been made, the anesthesiologist was informed of the identity of the study drug, and a bolus of 1.5 mg·kg$^{-1}$ propofol, followed by a bolus of vecuronium bromide, 0.2 mg·kg$^{-1}$, was given to facilitate tracheal intubation. Anesthesia was maintained by isoflurane, 0.5%–1%, and oxygen, 35%, with a nitrous oxide mixture, as well as incremental administration of the study drug.

### *Statistical analysis*

Pilot data were obtained from eight patients ($n = 4$ in each group). Power analysis based on the data indicated that eight subjects in each group were sufficient to detect a 50% difference (alpha = 0.05; beta = 0.2) in sensory block at 20 min after administration. The numbers of patients with sensory block in the L2, S1, or S3 dermatome at 10, 20, and 35 min after injection were compared between the two groups, using the $\chi^2$ test. The spread of sensory block in the cephalad direction over time was examined in each group using Wilcoxon rank order correlation. The Mann-Whitney *U* test was applied to examine the significance of the difference in cephalad levels of sensory block between the two groups. Further, in each group, the relationship between the presence of sensory block in the sacral region and the cephalad level of sensory block was examined by the Kruskal-Wallis test. Significance was set at $P < 0.05$.

## Results

All subjects were able to complete the study. One female patient in group R complained of nausea, and she had bradycardia due to vagal reflex at 15 min after the injection of ropivacaine. Upon the administration of a bolus of 0.5 mg atropine sulfate, her heart rate recovered to the baseline level. The background characteristics of the patients in the two groups did not significantly differ, except for the height of the patients (Table 1). At 10, 20, and 35 min after administration of the respective study drugs, there were no significant differences in the cephalad levels of sensory block to cold, pinprick, or touch between the two groups (Table 2).

### *Sensory block to cold* (Fig. 1)

At 10 min after administration of the respective study drug, the number of patients who obtained sensory block to cold in the L2, S1, or S3 dermatome did not significantly differ between groups R and M. At 20 and 35 min, significantly higher numbers of patients in group R obtained sensory block to cold in the S1 dermatome than in group M, whereas there were no significant differences in the numbers of patients who obtained sensory block to cold in the L2 or S3 dermatome between groups R and M.

### *Sensory block to pinprick* (Fig. 2)

There were no significant differences in the numbers of patients who obtained sensory block to pinprick in the L2 or S3 dermatome, either at 20 mins or at 35 min after administration between groups R and M. However, in the S1 dermatome, significantly higher numbers of patients in group R obtained sensory block to pinprick at 20 and 35 min than in group M.

### *Sensory block to touch* (Fig. 3)

A significantly higher number of patients in group R obtained sensory block to touch in the S3 dermatome at

**Table 1.** Patient characteristics

| | Group M ($n = 9$) | Group R ($n = 9$) | *P* |
|---|---|---|---|
| Age, in years; median (range) | 42 (27–59) | 46 (35–61) | NS |
| Height, in cm; mean ± SD | 155 ± 6 | 160 ± 6 | <0.05 |
| Weight, in kg; mean ± SD | 53 ± 9 | 60 ± 8 | NS |
| Sex (M:F) | 1:8 | 3:6 | NS |

NS, not significant; group M, 2% mepivacaine; group R, 1% ropivacaine

**Table 2.** Vital signs and cephalad levels of sensory block

| | | Group M ($n = 9$) | Group R ($n = 9$) | $P$ |
|---|---|---|---|---|
| Vital signs | | | | |
| Systolic blood pressure | Baseline | 127 ± 16 | 130 ± 20 | NS |
| (mmHg); mean ± SD | 10 Min | 121 ± 10 | 114 ± 20 | NS |
| | 20 Min | 114 ± 10 | 107 ± 19 | NS |
| | 35 Min | 111 ± 12 | 105 ± 17 | NS |
| Heart rate (eats·min$^{-1}$); | Baseline | 79 ± 12 | 75 ± 10 | NS |
| mean ± SD | 10 Min | 86 ± 15 | 76 ± 8.5 | 0.04 |
| | 20 Min | 86 ± 11 | 75 ± 9 | 0.005 |
| | 35 Min | 84 ± 10 | 72 ± 5 | 0.004 |
| Cephalad level of sensory block | | | | |
| Cold; median (range) | 10 Min | T5 (T6–T4) | T4 (T6–T4) | NS |
| | 20 Min | T4 (T6–T4) | T4 (T6–T4) | NS |
| | 35 Min | T4 (T4–T2)* | T4 (T6–T2) | NS |
| Pinprick; median (range) | 20 Min | T6 (T6–T4) | T4 (T8–T4) | NS |
| | 35 Min | T4 (T6–T4) | T4 (T6–T4) | NS |
| Touch; median (range) | 20 Min | T7 (T8–T4) | T6 (T8–T4) | NS |
| | 35 Min | T6 (T6–T4) | T6 (T6–T4)** | NS |

* $P = 0.02$ versus 10 min in the same group; ** $P = 0.04$ versus 20 min in the same group
Group M, 2% mepivacaine; group R, 1% ropivacaine

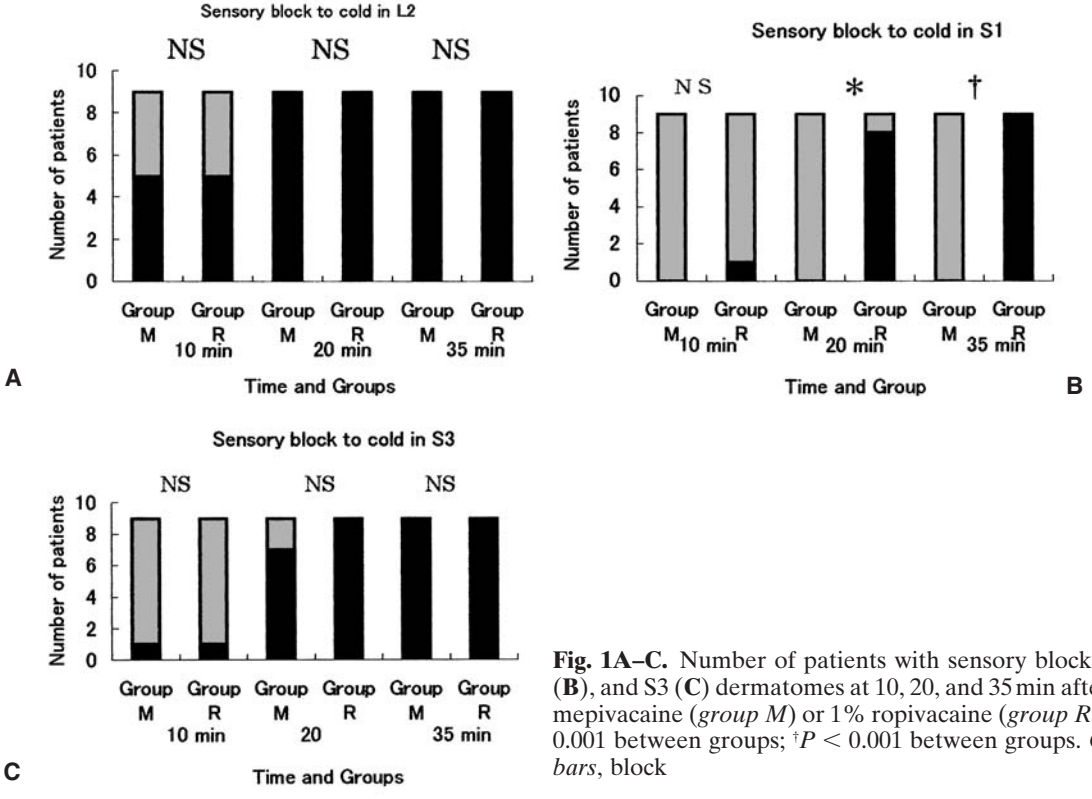


**Fig. 1A–C.** Number of patients with sensory block to cold in the L2 (**A**), S1 (**B**), and S3 (**C**) dermatomes at 10, 20, and 35 min after epidural injection of 2% mepivacaine (*group M*) or 1% ropivacaine (*group R*). *NS*, not significant; *$P = 0.001$ between groups; †$P < 0.001$ between groups. *Gray bars*, no block; *black bars*, block

35 min than in group M. However, the numbers of patients with sensory block to touch in the L2 dermatome at 20 and 35 min and in the S3 dermatome at 20 min did not significantly differ between groups M and R. No patient in either group obtained sensory block to touch in the S1 dermatome at 20 min or at 35 min after injection.

## Discussion

In the present study, 1% ropivacaine administered in the lower thoracic epidural space produced sensory block in the S1 dermatome in a significantly higher number of patients compared with 2% mepivacaine. Within 35 min, all patients in group R had attained sen-

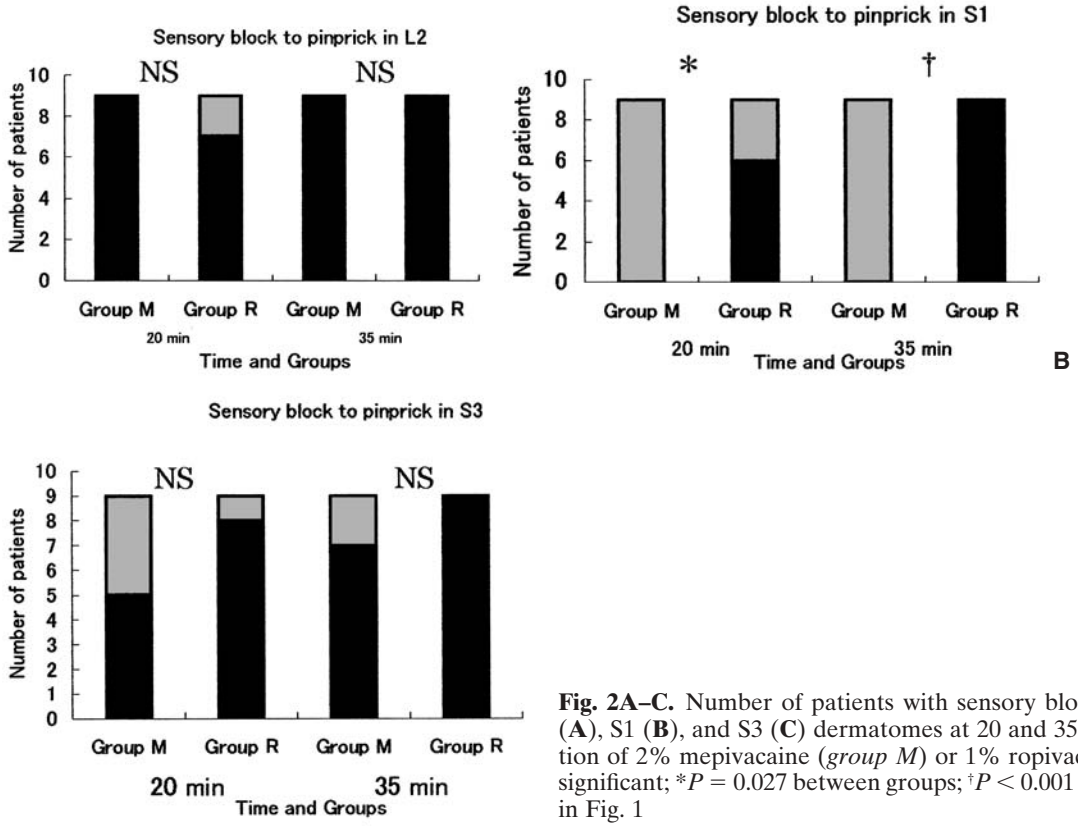


**Fig. 2A–C.** Number of patients with sensory block to pinprick in the L2 (**A**), S1 (**B**), and S3 (**C**) dermatomes at 20 and 35 min after epidural injection of 2% mepivacaine (*group M*) or 1% ropivacaine (*group R*). *NS*, not significant; $^{*}P = 0.027$ between groups; $^{\dagger}P < 0.001$ between groups. *Bars*, as in Fig. 1

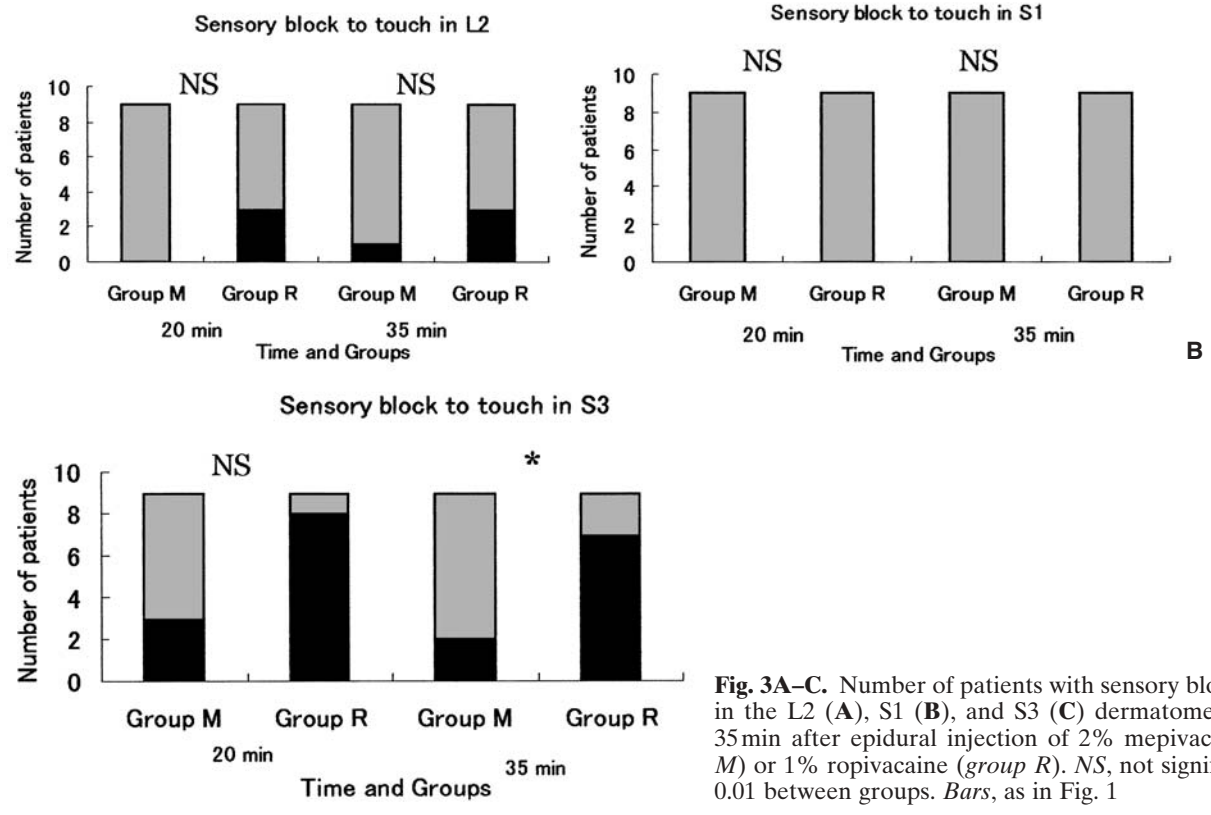


**Fig. 3A–C.** Number of patients with sensory block to touch in the L2 (**A**), S1 (**B**), and S3 (**C**) dermatomes at 20 and 35 min after epidural injection of 2% mepivacaine (*group M*) or 1% ropivacaine (*group R*). *NS*, not significant; $^{*}P = 0.01$ between groups. *Bars*, as in Fig. 1

sory block to cold and pinprick in the S1 dermatome. The cephalad level of sensory block was comparable between the two groups.

The reason for the difference in sensory block may be due, in part, to a difference in potency between the two drugs. A local anesthetic administered in the epidural space crosses into the subarachnoidal space via dural root sleeves and exerts its primary action on spinal roots and spinal-cord tracts [8]. The concentration of a local anesthetic in the CSF during epidural administration is similar to that during spinal anesthesia [9]. The total dose of local anesthetics administered in the epidural space is the primary determinant of the intensity of epidural anesthesia [10]. Because we injected either one of two drugs that have different potencies, we administered different volumes of each drug. A clinical study demonstrated that 1% ropivacaine induced patterns of sensory blockade and motor block that were similar to those induced by the same volume of bupivacaine 0.75% [11]. Another study indicated that ropivacaine, 0.75%, had the same potency as the same volume of 0.5% bupivacaine [12]. A clinical study indicated that 2% mepivacaine produced a block identical to that produced by 0.5% bupivacaine [6]. Thus, a 12-ml bolus of 1% ropivacaine, which we had chosen, may have the same potency as an 18-ml bolus of 2% mepivacaine. Groups M and R in our study had nearly identical levels of cephalad spread of sensory blockade to cold, pinprick, and touch, indicating that the intensity of block produced by the two drugs may be nearly identical, except at the S1 dermatome. The difference in potency of the two drugs may not be the main reason for the differences at the S1 dermatome.

Another possible explanation for the differences at the S1 dermatome is that there may be a difference in the chemical properties of the two drugs. Nearly all patients in the present study, including those in group M, obtained sensory block to cold and pinprick in the S3 dermatome during the observation period, showing no significant differences between the two groups. As for the first sacral nerve, which has a large diameter (making it resistant to local anesthetics) the amount of a drug around the spinal root in the dural cuff or around the spinal cord in the subarachnoidal space may be important in establishing an anesthetic action. Earlier development of sensory block in the S1 dermatome upon lumbar epidural administration of lidocaine-bicarbonate compared with lidocaine alone indicated the contribution of the type of local anesthetic towards penetration of the dura [13]. Bernards and Hill [14] reported that there was a biphasic relationship between the octanol/buffer distribution coefficient and a drug's permeability through the meninges. The bioavailability of lidocaine in the CSF upon epidural administration of lidocaine was unexpectedly greater than that of bupivacaine, even though lidocaine is more hydrophilic than bupivacaine [15]. These basic studies suggest that the lipophilicity of a local anesthetic administered in the epidural space may contribute to the extent of penetration through the spinal meninges. The octanol/buffer distribution coefficient of mepivacaine was reported to be 21 [16]. The octanol/buffer distribution coefficient of ropivacaine is 121, and is nearly identical to that of alfentanil, which possesses the highest permeability coefficient among clinically usable opioids and local anesthetics [14,16]. This difference indicates that ropivacaine may possess a high ability to diffuse through the dura or spinal meninges to the CSF. It is likely that a difference in the lipophilicity of mepivacaine and ropivacaine caused the differences observed between groups M and R. A study that reported the cross-sectional areas of nerve roots indicated that the spinal roots occupying the largest amount of space at L1 and L2 may become a partial barrier in the CSF to the diffusion of local anesthetics after the anesthetics penetrate the dura [2]. In the present study, a local anesthetic was administered at a level cephalad to the L1 dermatome. The total mass of drug that reached the sacral level may be less than the total mass of drug that reached the blocked dermatome at the cephalad level. A smaller amount of each drug than the amounts we calculated may have produced sensory block in the S3 dermatome in group M or group R; however, in the S1 dermatome, which possesses nerve fibers with the largest diameter, the amount of mepivacaine may have been too low to exert a sensory blocking action in group M. A significantly higher number of patients in group R obtained sensory block to touch in the S3 dermatome at 35 min than in group M. However, the level of sensory block to touch induced by a local anesthetic shows wide interindividual variability compared with the level of sensory block to cold or pinprick [17]. The reduction in the number of patients who maintained sensory block to touch in the S3 dermatome over time indicates that, in the present study, there may have been a bias for sensitivity to sensory block to touch.

It is not known whether an even lower concentration of ropivacaine than that used by us produces sensory blockade in the S1 dermatome. Peripheral sensitization of visceral afferents may occur due to the release of proinflammatory molecules such as bradykinin, tachykinin, and prostaglandins at the site of injury [18]. Leung et al. [19] have reported that pre-incision skin infiltration of local anesthetics during hysterectomy did not contribute to postoperative analgesia, because the pain had a visceral or somatic origin. Mihic and Abram [20] reported that the optimal regional anesthesia for hysterectomy was combined spinal and epidural anesthesia, for the reason noted by Leung et al. [19]. These studies suggest that the blockade of visceral pain during

and after surgery may contribute to the level of postoperative pain. The present study indicates that the injection of 1% ropivacaine may provide better quality of analgesia during surgery than 2% mepivacaine.

In conclusion, 1% ropivacaine produced sensory blockade in the S1 dermatome more frequently than 2% mepivacaine.

## References


1. Rud J (1961) Local anesthetics: an electrophysiological investigation of local anesthesia of peripheral nerves with special reference to xylocaine. Acta Physiol Scand 51 [Suppl]:1–171
2. Hogan Q (1996) Size of human lower thoracic and lumbosacral nerve roots. Anesthesiology 85:37–42
3. Galindo A, Hernandez J, Benavides S, Ortegon de Munoz, Bonica JJ (1975) Quality of spinal extradural anaesthesia: the influence of spinal nerve root diameter. Br J Anaesth 47:41–46
4. Cousins M (1989) Acute postoperative pain. In: Wall PD, Melzack R (eds) Textbook of pain, 2nd edn. Churchill Livingstone, Oxford, pp 284–305
5. Markham A, Faulds D (1996) Ropivacaine: a review of its pharmacological and therapeutic use in regional anesthesia. Drugs 52:429–449
6. Kaneko T, Iwama H (1999) The association between injected volume of local anesthetic and spread of epidural anesthesia: a hypothesis. Reg Anesth Pain Med 24:153–157
7. Liu SS, Ware PD, Rajendran S (1997) Effects of concentration and volume of 2-chloroprocaine on epidural anesthesia in volunteers. Anesthesiology 86:1288–1293
8. Wood MB, Rubin AP (1993) A comparison of epidural 1% ropivacaine and 0.75% bupivacaine for lower abdominal gynecologic surgery. Anesth Analg 76:1274–1278
9. Finucane BT, Sandler AN, Mckenna J, Reid D, Milner AL, Friedlander M, Muzyka D, Callaghan-Enright SO, Chan V (1996) A double-blind comparison of ropivacaine 0.5%, 0.75%, 1.0% and bupivacaine 0.5%, injected epidurally, in patients undergoing abdominal hysterectomy. Can J Anaesth 43:442–449
10. Boidin MP, Sulimma H (1991) Fentanyl in 2% mepiracaine compared with fentanyl in 0.5% bupivacaine: two parallel controlled double blind studies. Acta Anaesth Belg 42:93–99
11. Shantha TR, Evans JA (1972). The relationship of epidural anesthesia to neural membranes and arachnoid villi. Anesthesiology: 543–557
12. Bromage PR (1975) Mechanism of action of local anesthetics. Br J Anaesth 47:199–211
13. Arakawa M, Aoyama Y, Ohe Y (2002) Epidural bolus injection with alkalinized lidocaine improves blockade of the first sacral segment—a brief report. Can J Anaesth 49:561–570
14. Bernards CM, Hill HF (1992) Physical and chemical properties of drug molecules governing their diffusion through the spinal meninges. Anesthesiology 77:750–756
15. Clement R, Malinovsky, Le Colle P, Dollo G, Chevanne F, Le Vergo R (1999) Cerebrospinal fluid bioavailability and pharmacokinetics of bupivacaine and lidocaine after intrathecal and epidural administration in rabbits using microdialysis. J Pharmacol Exp Ther 289:1015–1021
16. Tucker GT, Mather LE (1998) Properties, absorption, and disposition of local anesthetic agents. In: Cousin MJ, Bridenbaugh PO (eds) Neural blockade in clinical anesthesia and management of pain, 3rd edn. Lippincott-Raven, Philadelphia, pp 55–95
17. Liu SS, Ware PD (1997) Differential sensory block after spinal bupivacaine in volunteers. Anesth Analg 84:115–119
18. Bueno L, Fioramonti J, Garcia-Villar R (2000) Pathobiology of visceral pain: molecular mechanisms and therapeutic implications. III. Visceral afferent pathways: a source of new therapeutic targets for abdominal pain. Am J Physiol Gastrointest Liver Physiol 278:C670–C676
19. Leung CC, Chan YM, Ngai SW, Ng KF, Tsui SL (2000) Effect of pre-incision skin infiltration on post-hysterectomy pain—a double blind randomized controlled trial. Anaesth Intensive Care 28: 510–516
20. Mihic DN, Abram SE (1993) Optimal regional anaesthesia for abdominal hysterectomy: combined subarachnoid and epidural block compared with other regional techniques. Eur J Anaesth 10:297–301